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TRANSIENT HYPERTENSION

THE RELATIVE PROGNOSTIC IMPORTANCE OF VARIOUS SYSTOLIC AND DIASTOLIC LEVELS

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In the preceding paper in this series,[1] based on an analysis of the medical records of 22,741 officers of the United States Army, the significance of transient hypertension was considered in terms of the subsequent state of health and the cause of death. A comparison was made between those who exhibited temporary elevations of blood pressure and those with normal levels throughout the periods of observation. The group with transient hypertension showed a greater incidence of later sustained hypertension and higher rates for disability retirement and death with cardiovascular-renal diseases.[2] It is thus apparent that, in many persons, a temporary rise in blood pressure, even though this occurs under emotional stress, must be regarded as of consequence; it is often an early sign of disorder in the circulatory system.

In the study just mentioned, the group with transient hypertension was dealt with as a whole; there was no attempt to ascertain possible differences in the prognostic importance of various systolic and diastolic levels. To obtain data on this point seemed the next logical step in the inquiry. The results are given in the present report.

MATERIAL AND PROCEDURE

The sources of the records and the general composition of the material already have been published in detail.[3] A punch card was made for each of the 22,741 cases, so that manipulation for statistical purposes could be readily carried out. Cardiovascular-renal conditions, if present, were always tabulated as causes of retirement and death, even though not immediately responsible for either. For example, malignant disease may have been the reason for which an officer left the service; but if hypertension also was present, he was considered to have retired with this circulatory disorder. A similar procedure was followed in case of death.

In dealing with data of this sort, age is of fundamental importance. This factor has been taken into account by resorting to an analysis in terms of person-years of observation, as was described in a previous paper.[1]

For purposes of study, the subjects with transient hypertension were divided into groups according to the highest levels of blood pressure recorded during the period of observation. For the systolic, the groups were 151 to 165 and 166 to 225; for the diastolic, 91 to 100 and 101 to 150. There were no readings noted above 225 systolic and 150 diastolic. Every combination of systolic and diastolic pressure was given separate consideration so that, excluding the simultaneous occurrence of normal values for the two, there were eight categories in all. Further subdivision, by reducing the number in each group, would have lessened the value of the comparisons.

RESULTS

The fundamental results are summarized in table 4. Tables 1, 2 and 3, from which the various ratios of table 4 are derived, are reproduced merely to illustrate the method employed.

In table 1 is shown the number of person-years of observation in each age group before the occurrence of sustained hypertension, for the various degrees of transient hypertension. By far the most extensive observations pertain to the group with a normal systolic pressure and a minimal elevation of the diastolic; the least extensive are in the group with a high systolic and a normal diastolic. The latter combination, as might be expected, is relatively uncommon. The distribution in the other groups is fairly even. Similar distributions of person-years were tabulated for each group before the occurrence of retirement or death. In this table the length of the calculated overall period of observation is some 5 per cent larger than that indicated in table 1 because it includes the time from the onset of permanent hypertension to retirement or death. Although the table is not shown, it was used in the derivation of table 4.

This is the third in a series of papers dealing with "Studies of Blood Pressure in Army Officers."

Dr. John W. Fertig, professor of biostatistics, Columbia University College of Physicians and Surgeons, aided in the analysis and preparation of the material for final presentation.

The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Columbia University.

1. Levy, R. L.; Hillman, C. C.; Stroud, W. D., and White, P. D.: Transient Hypertension: Its Significance in Terms of Later Development of Sustained Hypertension and Cardiovascular-Renal Diseases, J. A. M. A. **126**: 829 (Nov. 25) 1944.

2. By transient hypertension is meant a reading over 150 mm. of mercury systolic or 90 diastolic which is followed, on any particular examination or at a later examination, by a reading below these levels. The highest systolic and diastolic readings obtained in any one of a series, taken at a given examination, were recorded. Sustained hypertension is taken to mean a reading of over 150 systolic or 90 diastolic, persisting throughout an examination and not followed in subsequent examinations by lower levels.

3. Hillman, C. C.; Levy, R. L.; Stroud, W. D., and White, P. D.: Studies of Blood Pressure in Army Officers: Observations Based on an Analysis of the Medical Records of 22,741 Officers of the United States Army, J. A. M. A. **125**: 699 (July 8) 1944.

In table 2 are given the rates, in the subjects without transient hypertension, for the later occurrence of sustained hypertension, and of retirement and death with cardiovascular-renal diseases. These figures are taken from tables 2, 3 and 5 in an earlier paper.[1]

In table 3 appears the comparison, by age and for various degrees of transient hypertension, between the observed and expected number of cases of later sustained hypertension, of retirements and of deaths with cardiovascular-renal diseases. The expected number of cases was obtained by applying, at the various ages, the normal rates shown in table 2 to the corresponding age distribution of person-years, such as given in table 1. In each of the three categories of occurrences, the total observed number of cases exceeded that expected; and with only one exception, this relationship held for every combination of systolic and diastolic pressure.

In table 4 are shown the ratios for the observed to the expected number of cases of later sustained hypertension, as well as for retirements and deaths, by various levels of systolic and diastolic blood pressure. These ratios were calculated from the figures given in table 3.

The ratios for deaths with cardiovascular-renal diseases are, with one exception, all greater than unity. But they are not all significantly greater, nor do they show differences between the various levels of pressure, either for the systolic or for the diastolic. It is thus not clearly demonstrated that every transient elevation of blood pressure above the normal is important from the point of view of death with a circulatory disorder.

COMMENT

Very few attempts have been made to appraise the relative importance of various degrees of transient hypertension. In fact, only two pertinent references have been found. On the basis of the experience of the Prudential Insurance Company of America, MacKenzie and Shepherd [4] in 1937 stated that a systolic pressure of 150 mm. or more in the past required a rating, even though later pressures were normal; and a record of a previous systolic of 165 or over, with moderate elevation on subsequent examination, required a substantial rating or rejection. No similar information on diastolic pressures was available.

In 1940 Hines [5] reported the results of a study of 1,522 patients at the Mayo Clinic, of whom some were checked ten and some twenty years later. Only 243 (4.4 per cent) had blood pressure readings on the first examination of more than 145 mm. systolic and 90 diastolic. This initial elevation was assumed to be due to nervousness, since there was no evidence of vascular or renal disease. The following conclusions were drawn: Transient elevations of blood pressure above

TABLE 1.—*Person-Years Observed Before Occurrence of Sustained Hypertension, by Age, for Various Degrees of Transient Hypertension*

	Degree of Transient Hypertension, Mm. Hg							
	150 or Less	150 or Less	151-165	151-165	151-165	166-225	166-225	166-225
Age, Years	91-100	101-150	90 or Less	91-100	101-150	90 or Less	91-100	101-150
25-29	1,061	147	331	201	117	70	90	105
30-34	2,613	312	284	428	268	53	144	294
35-39	4,351	550	273	740	475	48	244	574
40-44	5,613	774	326	1,037	693	85	398	864
45-49	5,576	827	356	1,212	783	108	509	1,012
50-54	3,964	637	275	1,197	659	81	502	877
55-59	2,315	344	252	913	433	66	418	521
Total	25,493	3,591	2,097	5,728	3,428	511	2,305	4,237

With respect to the later development of sustained hypertension, it appears that all levels of transient hypertension, whether involving the systolic or diastolic or both, are relevant. The ratios for all levels of the systolic are so nearly alike that no emphasis can be placed on any one of them. In general, the ratio does not change significantly with a change in the systolic level, provided the diastolic remains constant. On the other hand, as the diastolic level rises while the systolic remains constant, the ratio does increase significantly. On closer analysis, however, it is evident that the ratios for the "90 or less" and the "91 to 100" groups do not differ from each other, but that both of these differ from the "over 100" group. The high ratio for this last group stands out prominently.

The same trends are evident in the case of retirements with cardiovascular-renal diseases. Here again, with one possible exception, every transient elevation above the normal, for both systolic and diastolic pressures, has a statistically significant ratio. After detailed analysis of the ratios, the same conclusion is reached as in the case of later sustained hypertension, namely that it is a diastolic reading above 100 which is of the greatest importance. Because of the small number of cases involved, not much attention should be given to the ratio obtained for the group 166 to 225 systolic, 90 or less diastolic.

TABLE 2.—*Rates for Sustained Hypertension, Retirements and Deaths, by Age, Among Those Without Transient Hypertension*

	Rate per Thousand Person-Years Observed		
	Later Occurrence of Sustained Hypertension	Cardiovascular-Renal	
Age, Years		Retirements	Deaths
25-29	0.45	0.16	0.23
30-34	0.87	0.23	0.09
35-39	1.67	0.51	0.14
40-44	2.57	1.38	0.38
45-49	5.74	3.92	1.24
50-54	9.68	10.34	2.10
55-59	14.90	22.49	5.16

4. MacKenzie, L. F., and Shepherd, P.: The Significance of Past Hypertension in Applicants Later Presenting Normal Average Blood Pressures, Proc. A. Life Insur. M. Dir. America **24**: 157, 1937.

5. Hines, E. A., Jr.: Range of Normal Blood Pressure and Subsequent Development of Hypertension: A Follow-Up Study of 1,522 Patients, J. A. M. A. **115**: 271 (July 27) 1940.

140 mm. systolic or 85 diastolic are prognostic of probable subsequent hypertension (defined as above 160 systolic and 100 diastolic); the higher the original reading, the higher the incidence of subsequent hypertension; rise in the systolic pressure alone is not indicative of subsequent hypertension; 85 mm. marks a critical level of the diastolic pressure as to the possible occurrence of subsequent hypertension.

TABLE 3.—*Observed Number of Cases of Sustained Hypertension, and of Retirement and Death, by Various Degrees of Transient Hypertension, Compared with That Expected on the Basis of the Rates for the Group Without Transient Hypertension* *

Degree of Transient Hypertension, Mm. Hg	Later Occurrence of Sustained Hypertension		Cardiovascular-Renal			
			Retirements		Deaths	
	Observed	Expected	Observed	Expected	Observed	Expected
150 or less / 91-100	372	129	248	136	75	33
150 or less / 101-150	84	19	62	22	9	5
151-165 / 90 or less	32	10	19	12	10	3
151-165 / 91-100	122	37	62	43	26	10
151-165 / 101-150	111	20	67	24	8	6
166-225 / 90 or less	14	3	12	3	2	1
166-225 / 91-100	48	16	26	19	2	4
166-225 / 101-150	139	26	87	30	20	7
Total	922	260	583	289	152	69

* The expected number of cases was obtained by applying, at the various ages, the normal rates shown in table 2 to the observed age distribution of person-years, such as that given in table 1.

Our own study is characterized by being based on the records of a relatively large number of persons followed over long periods of time and by the fact that annual examinations were made. In addition, in all of the calculations age and the period of follow-up were taken into account by using the method of person-years. For these reasons, direct comparison of our results with those so far reported by others is not feasible.

Certain features merit special mention. It is clear that all levels of transient hypertension, as here defined, are significant. This obtains for both the systolic and the diastolic pressure, using as indexes the later development of sustained hypertension and retirement with cardiovascular-renal diseases. Of particular interest is the observation that slight degrees of elevation are important, even when the systolic level alone is involved. Outstanding, however, and of the greatest significance, is a transient rise in the diastolic pressure above 100 mm., especially as far as this may be an early sign of subsequent sustained hypertension.

It has already been pointed out that, in the group with transient hypertension as a whole, the death rate with cardiovascular-renal diseases was significantly higher than in the group with normal pressures. Yet no real differences were apparent between the rates pertaining to the various degrees of elevation. This may be explained in part by the relatively small number of deaths involved. But it may be due also to the unpredictable course of hypertensive vascular disease, once this has been established. Prognostic criteria, except in the advanced stages, are uncertain and frequently deceptive. So too the degree of transient hypertension does not serve to foretell the severity and extent of the condition which eventually is a cause of death.

SUMMARY AND CONCLUSIONS

1. In an earlier paper, based on an analysis of the medical records of 22,741 officers of the United States Army, it was shown that in the group with transient hypertension there was a greater incidence of later sustained hypertension and there were higher rates for retirement and for death with cardiovascular-renal diseases. Using the same material and indexes, the present study was designed to demonstrate possible differences in the prognostic importance of various systolic and diastolic levels of transient hypertension.

2. With respect to the later development of sustained hypertension and retirement with cardiovascular-renal diseases, all levels of transient hypertension, both systolic and diastolic, were significant. Of particular interest was the observation that slight degrees of elevation were important, even when the systolic level alone was involved. Of the greatest significance was a transient rise in diastolic pressure above 100 mm., especially as an early sign of subsequent sustained hypertension.

3. No significant differences were apparent between the various degrees of transient hypertension in relation to the death rates with cardiovascular-renal diseases. So, as is true for many other prognostic criteria applied to these conditions, the height of a temporary rise in blood pressure does not appear to foretell the severity or extent of the lesions which eventually are a cause of death.

4. The data given lend support to the view that transient elevations of blood pressure, above the upper range of normal, often represent an early stage of hypertensive vascular disease.

TABLE 4.—*Ratio of Observed to Expected Number of Cases of Later Sustained Hypertension, and of Retirement and Death with Cardiovascular-Renal Diseases, by Various Levels of Systolic and Diastolic Blood Pressure* *

Later Development of Sustained Hypertension

B. P. Level, Mm. Hg		Diastolic 90 or Less	Diastolic 91-100	Diastolic 101-150
Systolic	150 or less	(1.0)	2.9	4.4
	151-165	3.2	3.3	5.5
	166-225	4.7	3.0	5.3
Average ratio †		3.5	3.0	5.1

Retirements with Cardiovascular-Renal Diseases

B. P. Level, Mm. Hg		Diastolic 90 or Less	Diastolic 91-100	Diastolic 101-150
Systolic	150 or less	(1.0)	1.8	2.8
	151-165	1.6	1.4	2.8
	166-225	4.0	1.4	2.9
Average ratio †		2.1	1.7	2.8

Deaths with Cardiovascular-Renal Diseases

B. P. Level, Mm. Hg		Diastolic 90 or Less	Diastolic 91-100	Diastolic 101-150
Systolic	150 or less	(1.0)	2.3	1.8
	151-165	3.3	2.6	1.3
	166-225	2.0	0.5	2.9
Average ratio †		3.0	2.2	2.1

* These ratios were derived from the figures given in table 3.
† These averages are based on the totals of the observed and expected cases involved.

THE USE OF HUMAN IMMUNE SERUM GLOBULIN (GAMMA GLOBULIN)

IN INFECTIOUS (EPIDEMIC) HEPATITIS IN THE MEDITERRANEAN THEATER OF OPERATIONS

I. STUDIES ON PROPHYLAXIS IN TWO EPIDEMICS OF INFECTIOUS HEPATITIS

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Prior to the report of Stokes and Neefe [1] indicating the value of gamma globulin from pooled human plasma in the prevention and attenuation of infectious (epidemic) hepatitis, no method of control of outbreaks of this disease had been available. The extensive literature on infectious (epidemic) hepatitis that has accumulated in the past several years bears witness to the widespread occurrence of this disease both in the armed services and among civilian populations. The lengthy period of convalescence following infectious hepatitis has made it of prime importance to the armed services of all the United Nations.

On the basis of the report of Stokes and Neefe and on the recommendation of the Surgeon General, U. S. Army, and at the invitation of the Chief Surgeon and the Commanding General, Mediterranean Theater of Operations, U. S. Army, to two of the authors of this present report, field studies on the effectiveness of gamma globulin [2] in the prevention of infectious hepatitis were conducted during the fall of 1944 and the winter of 1944-1945 in the Mediterranean Theater of Operations, U. S. Army. A heavy bombardment group with a relatively high incidence of infectious hepatitis was chosen at the suggestion of Col. Marion H. Barker, M. C., and Lieut. Col. Ross Gauld, M. C., and with the concurrence of Col. William S. Stone, M. C., and Col. Otis Benson, M. C., for the initial testing of the gamma globulin.

This bombardment group consisted of four squadrons and headquarters personnel. The four squadrons were of approximately equal size (each about 500 men) and were quartered around the same air field. Despite the fact that the study was begun late in the course of the outbreak of the disease, the group appeared highly suitable for investigation since its location was fixed and its rate of replacement was low. The number of cases of hepatitis with jaundice in the various squadrons of this group up to the time of injection of globulin is summarized in table 1.[3]

Squadrons A and C were chosen for globulin administration, while Squadrons B and D served as controls. Because of its large number of key personnel, the headquarters group also received globulin. As a result of the inclusion of the headquarters group, the number injected exceeded the number of controls by over 100 men.

TABLE 1.—*Cases of Hepatitis with Jaundice Previous to Globulin Injections*

	Head-quarters	Squadron A	B	C	D
Aug. 15 to Sept. 30	2	23	32	6	14
Oct. 1 to Oct. 31	1	13	19	9	9
Nov. 1 to Nov. 27	1	20	30	4	12
Total	4	56	81	19	35

Over a two day period, beginning on Nov. 27, 1944, a total of 10 cc. of globulin was given intramuscularly in the buttocks to each man in the injected squadrons. A few men, however, failed to receive the injections. The 10 cc. dosage was chosen as the largest that could be administered without adversely affecting full duty status of the men. No reactions followed administration of the globulin except for an occasional mild burning sensation at the site of injection.

Cases of hepatitis without jaundice were not included in the evaluation of the effectiveness of globulin. This form of hepatitis may be confused with various other diseases, and it was felt that by limiting the study to hepatitis with jaundice the conditions of the experiment were made more exacting.

In table 2 are recorded the cases of hepatitis with jaundice which occurred in the period from December 3 to January 26, following the date of injection. Cases which occurred between November 27 and December 1944 are not included, because of previous experience which had indicated that globulin when administered very late in the incubation period failed to prevent completely the development of the disease.

Thus in the injected squadrons 3 cases of hepatitis with jaundice occurred following the administration of globulin. In 2 of the 3 cases globulin had not been administered. The third case, with evidence of scleral icterus only, occurred nine days following the injection of globulin. In the same period 25 cases of hepatitis with jaundice occurred in the control squadrons.

TABLE 2.—*Cases of Hepatitis with Jaundice Occurring from Dec. 3, 1944 to Jan. 26, 1945 in Injected Men and Controls*

	Control Squadrons		Injected Squadrons		
Date	B	D	A	C	HQ
Dec. 3 to 8	3	1	..	..	1
Dec. 9 to 15	2	1	..	..	..
Dec. 16 to 22	3	..	..	..	..
Dec. 23 to 29	3	..	..	..	..
Dec. 30 to Jan. 5	2	..	..	..	..
Jan. 6 to 12	4	1	..	..	..
Jan. 13 to 19	2	1	1*	1*	..
Jan. 20 to 26	2	..	..	..	..
Total	21	4	1*	1*	1

* Failed to receive globulin.

This work was carried out under the direction of the Commission on Measles and Mumps of the Army Epidemiological Board, Preventive Medicine Service, Office of the Surgeon General, U. S. Army.

1. Stokes, J., Jr., and Neefe, J. R.: The Prevention and Attenuation of Infectious Hepatitis by Gamma Globulin, J. A. M. A. **127**: 144 (Jan. 20) 1945.

2. The gamma globulin used in these studies was obtained from pools of plasma, each pool representing 3,000 to 5,000 individuals, collected by the American Red Cross and fractionated, according to the method of Cohn and his co-workers, by various biologic manufacturers. These pools were obtained originally from groups of individuals in the Eastern and Southern regions of the United States.

3. The selection of squadrons for the injected and control groups was based on the reports of the total number of cases of hepatitis. When it was possible later to examine more complete data it was found that, while the total number of cases of hepatitis had been approximately equal in the injected and control groups previous to the time of injection, the cases of hepatitis with jaundice as indicated had not been equal. The experiment was thus weighted slightly in favor of the injected group, but not sufficiently so to account for the difference obtained.

With the extension of the disease in the Mediterranean Theater of Operations the opportunity arose to conduct a similar study in the ground forces.[4] Regiments were selected in which the disease had already started, and three groups of men from various companies of these regiments were chosen for the study. In group 1 406 men, 40 per cent of the strength of the companies forming the group, received globulin; the remaining men, 683, served as controls. In group 2 831 men, 10 per cent of the strength of the companies selected, were injected; 8,270 men remained for controls. In group 3 495 men, 25 per cent of the strength, were injected, the remaining 1,373 serving as controls. Each man injected received 10 cc. of gamma globulin intramuscularly. Group 1 was then studied for twelve weeks, group 2 for seven weeks and group 3 for five weeks following the date of injection.

In table 3 are recorded the cases of hepatitis with jaundice which occurred in the three groups during the follow-up period.

The significant results obtained in the foregoing studies suggest that gamma globulin is a potent agent in the prevention of infectious hepatitis. It is impossible to draw conclusions from these studies as to the duration of immunity conferred by globulin, but the results suggest that it may be a period of at least six to eight weeks.

TABLE 3.—*Cases of Hepatitis with Jaundice Following Date of Injection with Globulin*

Group	Total Injected	Jaundice Cases	Incidence, per Cent	Total Controls	Jaundice Cases	Incidence, per Cent
1	406	4	1	683	25	3.7
2	831	3	0.4	8,270	283	3.4
3	495	2	0.4	1,373	27	2.0

COMMENT

The present studies, together with those reported previously,[1] indicate that human immune serum globulin (gamma globulin) has been effective in preventing infectious (epidemic) hepatitis with jaundice in three separate epidemics of the disease. Although the signs and symptoms of the disease in all three epidemics were similar and although two of the epidemics appeared in the Mediterranean Theater of Operations at approximately the same time, it is still possible, although not probable, that the etiologic agent in each epidemic was different. Irrespective of possible etiologic differences, it is clear that the gamma globulin was equally effective in all outbreaks of infectious hepatitis. Whether or not such globulin from large pools of blood from three to five thousand individuals is effective in prophylaxis against serum hepatitis, such as that caused by the yellow fever vaccine during the present war, is not clear and must await further experimental study.

SUMMARY

An outbreak of infectious (epidemic) hepatitis in a bombardment group based in the Mediterranean Theater of Operations and in various regiments of the ground forces in the same theater offered an opportunity to study the effectiveness of human immune serum globulin (gamma globulin) in the prevention of this disease.

The results of these two field studies support the findings of Stokes and Neefe that the gamma globulin is a potent agent in the prevention of such hepatitis and suggest that the globulin confers a period of passive immunity of at least six to eight weeks.

4. Col. Charles O. Bruce, M.C., and Lieut. Col. Ross Gauld, M. C., assisted in this investigation.

AN EPIDEMIC OF INFECTIOUS HEPATITIS APPARENTLY DUE TO A WATER BORNE AGENT

EPIDEMIOLOGIC OBSERVATIONS AND TRANSMISSION EXPERIMENTS IN HUMAN VOLUNTEERS

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The control of infectious (epidemic) hepatitis, the only pandemic disease of the present war, has been seriously handicapped by the lack of any conclusive evidence concerning its method or methods of transmission. In our recent report on the prevention and attenuation of infectious hepatitis by gamma globulin [1] there was brief mention of the epidemic in which the globulin was tested. The epidemiologic factors involved in that epidemic also were investigated, and subsequently transmission experiments in human volunteers, using materials obtained from the patients and the camp, were conducted in order to supplement and confirm the epidemiologic observations. The results of these investigations have provided information concerning the sources of the causative agent and at least one of the methods responsible for its transmission.

I. THE EPIDEMIC

The Camp.—The epidemic occurred in a summer camp for boys and girls located in an isolated area in the Pocono Mountains near Philadelphia. The boys' and girls' sections of the camp were not separated by any physical boundary but were relatively independent units because each section had its own office, kitchen, dining room, infirmary, staff and activities. However, considerable intermingling between some of the members of the two groups resulted from mixed social and athletic activities. The members of the camp group were all of homogeneous racial origin (Jewish) and came from many cities and towns in a number of different states. With few exceptions all

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From the Department of Pediatrics, University of Pennsylvania School of Medicine and the Hospital of the University of Pennsylvania.

This investigation was conducted under the Commission on Measles and Mumps, Board for the Investigation and Control of Influenza and Other Epidemic Diseases in the Army, Preventive Medicine Service, Office of the Surgeon General, U. S. Army, Washington, D. C.

This investigation was made possible through the continued assistance and cooperation of the owners of the camp. Dr. I. E. Brownstein, Dr. Simon Forman and Dr. S. S. Mintz supplied information concerning the early phases of the epidemic and assistance in the collection of specimens. Members of the camp group and the many family physicians provided case data, obtained and delivered specimens and reported new cases among the camp group or their contacts. Other persons assisting in this part of the investigation included Miss Marion Thatcher, Miss Ruth Kennedy, Dr. James Woods, Dr. Robert Mayock and many members of Civilian Public Service Unit No. 140, Philadelphia.

The use of human volunteers for the transmission experiments was made possible by the cooperation of the administrative staffs of Selective Service (Camp Operations Division), the National Service Board for Religious Objectors, the American Friends Service Committee, the Philadelphia State Hospital and the New Jersey State Hospital. Members of Civilian Public Service Unit No. 140, Philadelphia, volunteered as subjects for these experiments. Many other members of C. P. S. Unit No. 140 assisted in analysis of the data, prepared the illustrations and assisted in many other ways in the conduct of parts of this investigation. John G. Reinhold, Ph.D., principal biochemist, Philadelphia General Hospital, gave advice, supervised the biochemical studies and prepared some of the materials used in the experiments. Mr. Charles Ming, Capt. Sydney S. Gellis, M. C., A. U. S., and Dr. Francis D. W. Lukens also assisted in the conduct of some phases of the investigation. Cooperation and assistance were given by the members of our laboratory staffs (Miss Dorothy Feinberg, Miss Arvilla Howley, Mrs. Jean Flick, Mrs. Mary Ming and Miss Catherine Fowler), Miss Dorothy Lanning and Miss Anne Messer of the biochemical laboratory of the Philadelphia General Hospital and members of the laboratory staff of the New Jersey State Hospital. The bacteriologic divisions of the laboratory of the New Jersey State Hospital and of the William Pepper Laboratories of Clinical Medicine of the Hospital of the University of Pennsylvania made the bacteriologic studies.

1. Stokes, J., Jr., and Neefe, J. R.: The Prevention and Attenuation of Infectious Hepatitis by Gamma Globulin, J. A. M. A. **127**: 144 (Jan. 20) 1945.

arrived at the camp on or about the opening date of June 30, 1944. After that time there was relatively little change in the camp population until the onset of the epidemic, although many friends and relatives visited. Prior to the epidemic, campers and counselors in the boys' and girls' sections numbered approximately 275 and 220 respectively. The campers ranged from 3 to 17 and the counselors from 17 to 30 years of age. Approximately 78 other persons, most of them under 40 years of age, completed the camp group.

Collection of Data.—For the sake of convenience in description of time relationships, the weeks following the opening date of camp have been numbered in sequence. We were notified [2] of the existence of this epidemic during the 7th week of the season, approximately two weeks after the start of the epidemic. Case data at that time were obtained from the records of the camp physicians and directors. Subsequent case data were obtained from the same source and by questionnaires which were sent to all members of the camp group. As many of them developed the disease after returning the first questionnaire and after they had returned home, a second set of questionnaires was sent to the entire group at a later date. The response to both sets of questionnaires was excellent. Since many of the group were from Philadelphia, additional data were obtained by telephone, from personal visits and from family physicians. When necessary, information was obtained by telephone concerning persons in other cities and towns.

Course of the Epidemic.—Three days after the opening of the camp (1st week) a woman (patient 1) aged 21, working in the office of the girls' section and living in cabin A, became ill with infectious hepatitis. During the 3d week an outbreak of "gastrointestinal upsets" occurred in the girls' section. As these were transient and usually did not require admission to the infirmary, complete records were not available. However, the section physician estimated that 25 to 30 per cent of the girls were involved, and the outbreak was of sufficient magnitude to lead him to institute special dietary measures for the entire female group. The outstanding symptom was nausea, headache was common, and vomiting and fever were present in some cases. Diarrhea was infrequent. Recovery occurred in twenty-four to forty-eight hours. A similar outbreak occurred during the 4th and 5th weeks in the boys' section.

During the 4th week and three and one-half weeks after the onset of hepatitis in the office worker, a female counselor (patient 2) developed the disease. This person also resided in cabin A and was closely exposed to case 1 during the 1st week. In the 5th week 2 more persons in the female group developed hepatitis. These persons lived in different cabins and had no unusual exposure to the first 2 cases. The epidemic nature of the disease became apparent during the 6th week, when 40 persons in the female group and 13 in the male group became ill with hepatitis. In both groups, campers and counselors living in different cabins were involved and the cases in the male group had had no recognized exposure to the early cases in the female group. In the following week the incidence in the male group rose sharply and that in the female group decreased. Additional cases continued to appear in the female and male groups until the end of the 12th and 13th weeks respectively, at which time the epidemic abruptly terminated.

TABLE 1.—*Total Incidence of Hepatitis at the Camp*

Group	Number	Hepatitis: With Overt Jaundice No.	%	Without Overt Jaundice No.	%	Total No.	%
Female group	265	139	53	43	16	182	69
Male group	308	116	38	52	17	168	55
Both groups	573	255	44	95	17	350	61

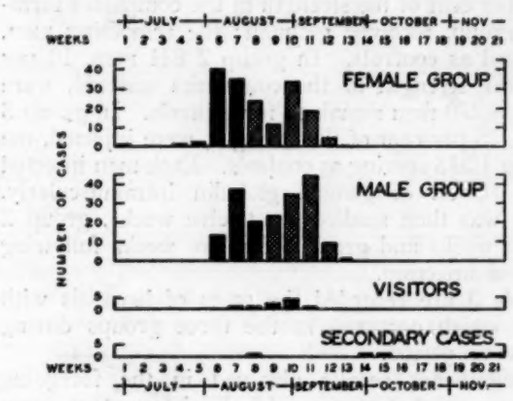

Chart 1.—Weekly incidence of hepatitis. The female and male groups include only those persons who resided in the female and male sections of the camp respectively. The group designated as visitors includes the persons who developed hepatitis after visiting the camp for only short periods. The group designated as secondary cases includes only those persons who had not visited the camp but developed hepatitis after exposure to infected persons from the camp. In respect to the female and male groups, solid bars have been used to indicate the number of persons developing the disease while at the camp, the cross hatched bars indicating the number developing their initial symptoms after leaving the camp. Although indicated by solid bars, in all of the visitors and secondary cases the disease developed away from the camp.

In table 1 the total incidence of hepatitis for the female and male groups is shown in terms of the number of cases and the percentage of the total group involved. The cases of hepatitis have been divided on the same basis according to the presence or absence of overt jaundice. The data show that the female group had the highest incidence of hepatitis even though the number of persons in this group was smaller than that in the male group. In respect to the combined groups, 350 (61 per cent) of the 572 persons contracted hepatitis during the thirteen weeks of the epidemic. Of the 350 cases, 344 occurred between the 6th and 12th weeks. None of these patients died. Forty-four per cent (255) of the total group of 572 persons developed overt jaundice, and 17 per cent (95) had hepatitis without overt jaundice. Thus 27 per cent of the hepatitis cases did not develop overt jaundice, giving a ratio of 2.7 to 1 of jaundiced to nonjaundiced cases.

As shown in chart 1, the weekly incidence curves of both the male and female groups showed two peaks. The highest weekly incidence in the female group is shown by the primary peak in the 6th week. The lower secondary peak occurred in the 10th week. The primary peak in the male group was in the 7th week. However, the highest weekly incidence in this group is reflected by the high secondary peak in the 11th week. Thus the majority of cases in the female group occurred during the early weeks of the epidemic period, whereas the majority in the male group occurred during the later weeks.

At least 9 persons who visited the camp for periods of two hours to several days at some time during the first six weeks developed hepatitis after three to six weeks. The total number of visitors to the camp is not known.

2. Dr. Charles L. Brown, professor of medicine and head of the Department of Medicine, Temple University School of Medicine, first was called in consultation by the camp directors for advice in connection with this epidemic. Dr. Brown, knowing of the interest of the Commission on Measles and Mumps in this disease, notified the director of the commission (J. S. Jr.) of the existence of the epidemic and of the desire of the camp directors for its investigation.

Since all of the girl campers and most of their counselors had returned to their homes by the end of the 7th week, and the entire camp group by the end of the 9th week, chart 1 shows that approximately 175 persons developed the disease at home after leaving camp. In addition, approximately 175 others in various stages of the disease had returned home with hepatitis. Follow-up inquiries were made at frequent intervals for four months after the camp had closed, and all of the members of the camp group were informed of the importance of reporting secondary cases among their contacts. Of the many relatives and friends, including many children, who had not visited the camp but subsequently were in close and prolonged contact in the various homes with approximately 350 infected persons from the camp, only 5 are known to have contracted hepatitis. Four of the 5 persons were relatives who lived in houses with persons infected at the camp. The 5th was a hospital nurse who was responsible for the care of one of the boy campers during the preicteric period of his disease. Considering the large number of persons exposed, the occurrence of only 5 secondary cases suggests that the agent was not easily acquired from infected persons away from the camp.

Diagnosis.—The differential diagnosis will be discussed in more detail in a subsequent report on other observations made in relation to this epidemic.[3] Briefly, the diagnosis of the disease as infectious hepatitis was based on the following points: (1) typical clinical picture and laboratory findings of infectious hepatitis; (2) absence of previous injections of homologous blood products and no opportunities for syringe or needle transmission of agent of serum hepatitis; (3) exclusion of Weil's disease by laboratory studies, which included dark field and electron microscopic examinations of serum, guinea pig inoculations, agglutination and complement fixation tests, leukocyte counts and microscopic urine examination; (4) absence of history of ingestion of hepatotoxic drugs or exposure to chemicals; (5) demonstration that the causative agent passed through a Seitz filter.

The diagnosis of infectious hepatitis without jaundice was made in patients presenting the same symptoms and signs as those who subsequently developed overt jaundice. Liver function studies on representative cases of the nonicteric group revealed bilirubinuria, increased urobilinogenuria, positive cephalin cholesterol flocculation tests and abnormal retention of sulfobromophthalein.

II. TRANSMISSION EXPERIMENTS IN HUMAN VOLUNTEERS

The transmission experiments will be considered first because the results assist in the subsequent discussions ("Epidemiologic Observations") of the possible sources of the causative agent and its method or methods of transmission at the camp. Because all attempts to cultivate the hepatitis agent in chick embryos and tissue cultures have been unsuccessful and no animal has been found to be susceptible, the only method of determining the presence of the agent in a given material is by demonstrating the ability of that material to produce the disease in human volunteers. It has been necessary, therefore, to use human beings for the transmission experiments.

A. METHODS AND MATERIALS

Volunteers.—The men who volunteered as subjects for these experiments were all under 35 years of age and had no previous history of jaundice and no evidence of liver dysfunction detectable by history, physical examination and liver function tests.

3. Neefe, J. R., and Stokes, J. Jr.: Infectious Hepatitis: Miscellaneous Observations on an Epidemic, to be published.

Studies on Volunteers.—Each subject was studied frequently by means of the group of liver function tests described in a previous report.[4] These included quantitative determinations of the serum concentrations of total bilirubin, total protein, albumin, globulin and total and esterified cholesterol; the serum cephalin cholesterol flocculation test; the thirty minute sulfobromophthalein test (5 mg. per kilogram dose), and urine tests for bilirubin (Harrison and diazo spot tests), urobilinogen (Wallace and Diamond) and urobilin (Schlesinger). These studies were made on each volunteer at frequent intervals during a one to three month preinoculation[5] period in order to determine the physiologic variation in the response of each one to these procedures over a period of time. After inoculation, most of these tests were carried out two to more times weekly up to six months. The same studies were conducted over the same interval of time on a group of 10 control subjects. In a few cases electrophoretic studies of the serum proteins were made on serum specimens collected before and after the onset of hepatitis. During the postinoculation period, groups inoculated with different materials were isolated from one another and the usual measures to prevent cross infection were instituted.

Materials.—Serum, nasopharyngeal washings, urine and feces were collected from many persons of the camp group in various stages of hepatitis. Serum and feces were also collected from volunteers who developed hepatitis following their inoculation with certain of the aforementioned materials. All specimens were examined bacteriologically, and any that contained bacteria other than the usual flora were discarded. These materials were all frozen within one to six hours after collection and were stored at minus 5 to minus 20 C. until used. In addition to the foregoing materials, water was obtained from one of the camp wells and flies were obtained from a fly trap in the boys' section of the camp. After thawing, certain specimens were pooled prior to their administration to human volunteers. The relationship of the specimens used in each pool to the times of onset of hepatitis in the donors is given in table 2, and the methods of collection of specimens and of preparation of the pools are discussed in connection with the results of their administration to volunteers (table 3).

TABLE 2.—*Time of Collection of Specimens Used in Pools in Relation to Time of Onset of Hepatitis in Donors*

Material	Weeks Before Onset: Number of Specimens					Weeks After Onset: Number of Specimens							Total Number of Specimens	Number of Patients Represented
	5	4	3	2	1	1	2	3	4	5	6	7		
Serum														
Pool 1 SIH	..	..	..	..	..	6	2	..	..	..	..	..	8	8
Pool 2 SIH	..	..	..	2	4	14	13	5	1	..	..	..	39	4
Nasopharyngeal washings														
Pool 1 NPIH	..	..	..	..	..	4	2	..	..	..	..	..	6	6
Pool 2 NPIH	..	..	1	1	1	10	5	1	1	..	..	..	20	20
Urine—Pool 1 UIH	1	..	..	..	1	11	11	3	2	4	3	2	38	38
Feces														
Pool 1 FIH	..	..	..	..	..	1	3	..	..	..	..	..	4	4
Pool 2 FIH	..	..	..	..	..	+	+	+	+	..	..	..	See text	2
Pool 4 FIH	..	..	..	..	..	5	9	..	..	..	..	..	14	3

B. RESULTS

The results of administration to volunteers of serum, nasopharyngeal washings, urine, feces, water and a preparation made from the flies were as follows (tables 2 and 3):

Serum.—Two serum pools[6] were prepared and administered to volunteers with the following results:

Pool 1 SIH: Single specimens were collected from 8 of the "camp hepatitis patients" during the first or second week after

4. Neefe, J. R.; Stokes, J., Jr.; Reinhold, J. G., and Lukens, F. D. W.: Hepatitis Due to Injection of Homologous Blood Products in Human Volunteers, J. Clin. Investigation **23**: 836 (Sept.) 1944.

5. The term "inoculation" is used herein to indicate the administration of potentially infectious materials regardless of the route.

6. Pools have been designated with code letters to simplify identification. Thus the code SIH indicates serum, infectious hepatitis; NPIH, nasopharyngeal washings, infectious hepatitis; FIH, feces, infectious hepatitis; UIH, urine, infectious hepatitis.

the onset of the disease. Three volunteers (group A) were injected parenterally with 1.1 cc. of this pool. These subjects have been observed for eleven months and no definite evidences of hepatitis have been detected.

Pool 2 SIH: This consisted of 39 specimens obtained from 4 volunteers before and after the onset of hepatitis produced experimentally by the oral administration of feces pool 1 FIH. Three volunteers (group B) received 3 cc. of this pool orally, and after twenty-six and thirty-three days respectively 2 developed infectious hepatitis with jaundice, indicating that the causative agent was present in this serum. However, 3 other subjects (group C) who were injected parenterally with 2.1 cc. of the same serum have shown no signs of hepatitis during the 132 days that have elapsed to date.

Nasopharyngeal Washings.[7]—Specimens were collected from many of the "camp hepatitis patients" by having them gargle with sterile saline solution or beef broth. Selected specimens were pooled and, without further treatment, two different pools were administered to two different groups of volunteers with the following results:

Pool 1 NPIH: Single specimens were collected from 6 patients during the first or second week after the initial symptoms of hepatitis. Approximately 4 cc. of this pool was sprayed and dropped into the nasopharynx of 3 volunteers (group D) on each of three successive days, a total volume of approximately 12 cc. being administered. No evidences of hepatitis have been detected during a period of eleven months.

Pool 2 NPIH: This consisted of single specimens collected from 20 patients during the preclinical,[8] preicteric, early, middle and late icteric stages of hepatitis. Six cc. was sprayed and dropped into the nasopharynx and 30 cc. was administered orally to each of 5 volunteers (group E). None have shown any evidence of hepatitis during a period of seven months.

Urine.—One large urine pool was prepared and administered to volunteers as follows:

Pool 1 UIH: Single specimens collected from 38 of the "camp hepatitis patients" in the preclinical, preicteric and early, mid and late icteric stages of the disease were pooled and, without further treatment, 25 cc. was administered orally to each of 7 volunteers (group F). No evidences of hepatitis have been detected in any of these men during a period of eight months.

Fly Extract.—In the 6th week of the camp season, during the first peak of the epidemic, a pint bottle was filled with living flies obtained from a fly trap located adjacent to the kitchen in the boys' section. The flies were killed within three hours by freezing. Later, after thawing, they were placed in buffered saline solution and subjected to the action of a Waring blendor. The resulting preparation was then filtered twice through a Berkefeld filter, and the filtrate produced no illness in mice, rats, guinea pigs or monkeys on intraperitoneal and intracerebral injection.[9]

Fifteen cc. of the filtrate (fly extract) was administered orally to each of 5 volunteers (group G). No evidence of hepatitis was detected in any of these men during a period of eight months.

Feces.—The following preparations were administered to volunteers:

Pool 1 FIH: Portions of 4 specimens collected from 4 of the "camp hepatitis patients" during the 1st or 2d week after the onset of the disease were pooled and approximately a 10 per cent suspension in distilled water was prepared by mixing the feces with distilled water in a Waring blendor. After being subjected to the action of the blendor for five to ten minutes, the suspension was strained through several layers of gauze and, after storage for several weeks at minus 5 to minus 20 C., was thawed and administered, without further treatment, to the volunteers.

Of 16 men (groups H, I and J) receiving 1.6 to 5 cc. of this pool orally, 11 developed infectious hepatitis after incubation periods of 18, 19, 19, 19, 21, 22, 22, 23, 24, 24 and 26 days. Ten of the 11 cases showed overt jaundice and, in these, the incubation periods did not exceed 24 days. The other, who had the longest incubation period in this group, had mild but definite hepatitis without jaundice. The mean incubation period for these 11 cases was 21.5 days.

The men of group K each ingested a volume of water which originally had contained approximately 1.5 cc. of feces pool 1 FIH. Before it was administered, this contaminated water was treated with coagulants and an adsorbent (sodium carbonate, aluminum sulfate and activated carbon) in an attempt to decrease the concentration of the hepatitis agent. The treatment procedure, described in detail elsewhere,[10] removed 85 per cent of the total organic solids in the specimen and made the water, formerly opalescent and pale brown, crystal clear. It seems certain, therefore, that the men of group K received considerably less than 1.5 cc. of feces pool 1 FIH. Two of the 5 men so inoculated developed mild infectious hepatitis, 1 with only scleral jaundice and the other without overt jaundice, after incubation periods of 33 and 37 days respectively.

TABLE 3.—*Results of Administration of Materials Obtained from Patients and from the Camp to Human Volunteers*

Material *	Amount, Cc.	Route	Subjects: Number	Subjects: Group	Results: No Illness	Results: Hepatitis: With Overt Jaundice	Results: Hepatitis: Without Overt Jaundice	Incubation Period, Days
Serum								
Pool 1 SIH	1.1	Parenteral	3	A	3	0	0	
Pool 2 SIH	3.0	Oral	3	B	1	2	0	26, 33
	2.1	Parenteral	3	C	3 †			
Nasopharyngeal washings								
Pool 1 NPIH	12.0	Nasopharynx	3	D	3	0	0	
Pool 2 NPIH	6.0	Nasopharynx						
	30.0	Oral	5	E	5	0	0	
Urine—Pool 1 UIH	25.0	Oral	7	F	7	0	0	
Fly extract	15.0	Oral	5	G	5	0	0	
Feces								
Pool 1 FIH	5.0	Oral	2	H	0	2	0	21, 23
	2.0	Oral	9	I	4	4	1	18, 22, 24, 24, 26
	1.6	Oral	5	J	1	4	0	19, 19, 19, 22
	<1.5*	Oral	5	K	3	1	1	33, 37
Seitz filtrate; pool 1 FIH	2.0	Oral	3	L	0	3	0	28, 30, 32
	1.0	Parenteral	3	M	3 †	0	0	
Pool 2 FIH	5.0	Oral	7	N	6	1	0	28
Water								
Water specimen GW	7000	Oral	5	P	1	0	4	61, 65, 66, 71
Feces pool 4 FIH ‡	10.0	Oral	5	R	4	0	1	54

* See text. † Results at time of writing (132 days); subject to change. ‡ Prepared from specimens obtained from group P.

7. The term nasopharyngeal washings has been used herein to indicate washings of the nasopharynx and of the oropharynx.

8. The term "preclinical" is used to indicate the period between infection and the first evidence, clinical or laboratory, of the disease.

9. The mice, rat and guinea pig tests of the fly extract and the Seitz filtrate of feces were made by Dr. Werner Henle, assistant professor of bacteriology in pediatrics, University of Pennsylvania School of Medicine. The tests of the same materials in monkeys were made by John F. Enders, Ph.D., associate professor of bacteriology and immunology, Harvard Medical School.

10. Neefe, J. R.; Stokes, J.; Baty, J. B., and Reinhold, J. G.: Disinfection of Water Containing the Causative Agent of Infectious (Epidemic) Hepatitis, this issue, p. 1076.

Seitz Filtrate of Pool 1 FIH: In order to determine whether the agent was filtrable, a portion of pool 1 FIH was passed through a Seitz filter. The filtrate was sterile on bacteriologic examination and produced no illness in mice, guinea pigs and monkeys. All of the 3 men (group L) receiving 2 cc. of this filtrate orally developed moderately severe to severe infectious hepatitis with jaundice after incubation periods of 28, 30 and 32 days. None of the 3 volunteers (group M) who received 1 cc. of the filtrate parenterally have developed infectious hepatitis to date (132 days).

Pool 2 FIH: This was prepared in the same manner as pool 1 FIH from portions of all specimens obtained from the men of group H during the first four weeks after the onset of hepatitis which followed their experimental inoculation with pool 1 FIH. One of the 7 volunteers (group N) who received orally 5 cc. of this pool developed hepatitis with jaundice after twenty-eight days.

Water.—On September 6, approximately two weeks after the camp had closed, specimens of water from both of the camp wells (see "Epidemiologic Observations") were collected in sterile containers, by the camp directors, for bacteriologic examination. The examination of the specimen obtained from the well in the girls' section revealed the presence of Escherichia coli, indicating fecal contamination. The specimen from the well in the boys' section was reported satisfactory for human consumption.

Collection and Storage of Water.—On October 6, 15 gallons of water was collected from the "girls' well" as follows: As water had not been pumped from this well after September 6, the water was allowed to run at full force (electric pump) for forty-five minutes from a faucet at the surface of the well. Each of three clean 5 gallon bottles then was rinsed thoroughly four times with water from the faucet, after which each bottle was filled with water, stoppered and transported to the laboratory. Circumstances did not permit a bacteriologic examination of these specimens until October 17, eleven days after collection. At that time Escherichia coli was isolated from each of the three bottles but no pathogenic intestinal bacteria were found. Owing to a lack of low temperature storage space, the water specimens were stored at room temperature in plain glass bottles, unprotected from light, in a laboratory from October 6 until November 5. On that date, thirty days after collection, approximately 12 liters of water from each of the three bottles was pooled (water specimen GW) and portions were ingested by volunteers (group P).

Criteria for Hepatic Dysfunction.—The significance of the changes that occurred in the responses of each of these men (group P) to the various liver function tests after inoculation has been evaluated by comparing them with their own preinoculation responses and also by comparing them with the results obtained in the control subjects. Such comparisons are permissible because the conditions of the experiment were uniform in respect to the inoculated and uninoculated groups and did not change throughout the period of observation. The occurrence of a single deviation from the normal in the results of one liver function test has not been regarded as significant evidence of hepatic dysfunction, because such sporadic deviations previously have been observed in supposedly normal persons or in patients with various conditions.[4] Deviations in the results of one test from the previously established normal response of that person have been regarded as evidence of hepatic dysfunction when persistent and associated with suggestive clinical manifestations or when associated with abnormal responses to one or more other tests of liver function. In order to determine the statistical significance of the changes observed in the men of group P during the postinoculation period, the normal responses of each person to the various tests, based on the studies made during the three month preinoculation period, have been calculated in terms of means and standard deviations. Values departing from the mean by more than twice the standard deviation were accepted as statistically significant deviations.

Experimental Conditions and Studies on Control Subjects.—The only variable between group P and a group of 10 control subjects confined under the same conditions in the same building throughout the period of the experiment was the ingestion of water specimen GW. The same series of liver function tests was conducted with the same frequency over the same period of time on the two groups. On the basis of these criteria, no significant indications of hepatic dysfunction were detected in the control subjects during the period of observation.

Results in Group P: On November 5, thirty days after collection, 7,000 cc. of water specimen GW was ingested by each of 5 volunteers (group P) over a period of thirty-six hours. Between the 61st and 71st days after the ingestion of this water, 4 of the 5 men developed mild illnesses characterized by nonspecific symptoms and signs associated with laboratory evidence of hepatic dysfunction. Since none of these men developed overt jaundice and because of the critical nature of this experiment, the data pertaining to the liver function tests on these men and the results of certain other related studies and experiments are presented:

(1) *Liver Function Studies.*—For convenience in description, the days after the ingestion of water specimen GW have been numbered in sequence.

W. H.: The liver function tests which showed deviations from the normal after the ingestion of water specimen GW are shown in chart 2. Sixty-five days after inoculation, the test for urine urobilinogen was positive in a urine dilution of 1 to 100 and the total serum bilirubin concentration had risen to

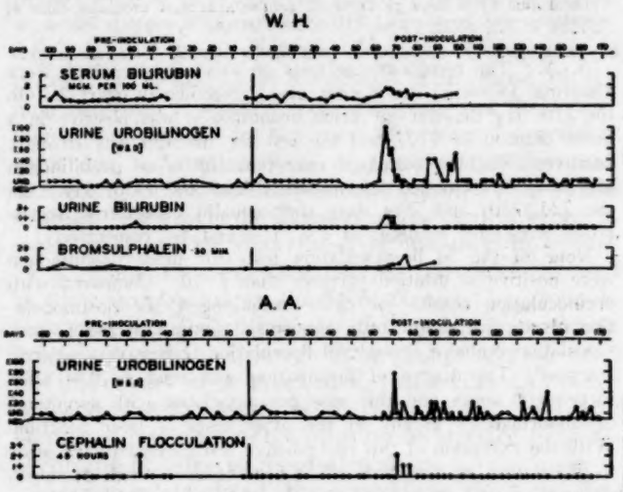

Chart 2.—Results of liver function tests in volunteers W. H. and A. A. before and after their inoculation with water specimen GW (water from well in girls' section of camp). Vertical line at 0 days indicates time of inoculation. Values for serum bilirubin indicate concentration of total serum bilirubin per hundred cubic centimeters. Urine urobilinogen readings represent highest dilution of urine with which positive reaction was obtained. Urines giving a positive reaction for urobilinogen with only the undiluted specimen are indicated at level UND on the ordinate. Urine bilirubin reactions are graded 0 to 4 plus. One plus urine bilirubin readings indicate that both the Harrison and the diazo spot tests were weakly but definitely positive. The results of sulfobromophthalein tests are expressed in percentage retention after 30 minutes. The cephalin cholesterol flocculation tests are read from 0 to 4+ depending on the degree of flocculation and clearing of the supernatant at 48 hours.

1.64 mg. per hundred cubic centimeters. The qualitative van den Bergh reaction was delayed direct and the tests for urine bilirubin were positive. The increased excretion of urine urobilinogen continued intermittently for thirty-four days, the maximum excretion being represented by a positive test with the 1:100 dilution. The total serum bilirubin concentration remained elevated for ten days, the values of the 67th, 68th and 75th days being 1.62, 1.54 and 1.44 mg. per hundred cubic centimeters respectively, all associated with delayed direct qualitative van den Bergh reactions. The tests for urine bilirubin continued to be positive until the 69th day. On the 75th day, sulfobromophthalein retention was 12 per cent at thirty minutes.

Based on the preinoculation studies, the normal response of W. H. to each of these procedures was as follows: (*a*) For 18 determinations of the total serum bilirubin concentration, the mean was 0.69 mg. per hundred cubic centimeters (S. D. ± 0.2; mean plus 2 S. D. — 1.09); (*b*) qualitative van den Bergh reaction (3 tests) negative; (*c*) the mean thirty minute sulfobromophthalein retention for 7 tests was 1.4 per cent (S. D. ± 1.9; mean plus 2 S. D. — 5.27); (*d*) urine urobilinogen

(25 tests) was never positive in dilutions of 1 to 10 or greater; (*e*) urine bilirubin was absent with 23 of 24 tests; the 1 test showed an atypical color reaction and was read as suggestive (±). Compared with these, the "postinoculation" results were significantly abnormal. On the basis of the criteria cited previously, the occurrence of significantly abnormal results with 4 liver function tests during the same period has been regarded as evidence of hepatic dysfunction.

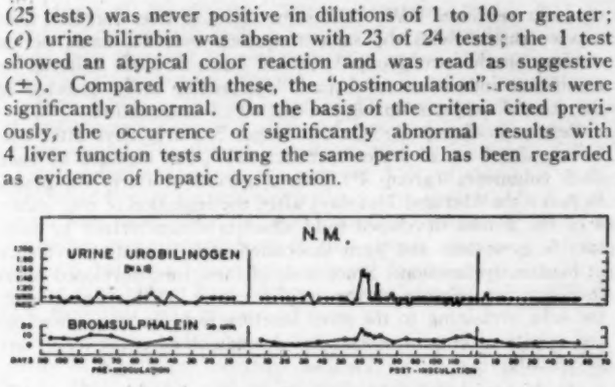

Chart 3.—Results of liver function tests in volunteers N. M. and E. V. before and after first inoculation with water specimen GW and after second inoculation with feces pool 1 FIH. Vertical line at 0 days to left of subject's initials indicates time of inoculation with water specimen GW. Vertical line at 0 days to right of subject's initials indicates time of inoculation with feces pool 1 FIH. See chart 2 for complete legend.

A. A.: The results of the tests on this subject, which were abnormal following inoculation, also are shown in chart 2. On the 71st day the test for urine urobilinogen was positive in a urine dilution of 1:75 and the test for urobilin was strongly positive. Slightly increased excretions of urine urobilinogen and urobilin continued intermittently until the 145th day. On the 72d, 75th and 78th days the cephalin cholesterol flocculation tests gave readings of 2+, 1+ and 1+ respectively.

None of the 30 preinoculation tests for urine urobilinogen were positive in dilutions greater than 1:10. Compared with preinoculation results for urine urobilinogen, the postinoculation results are significantly abnormal. Only 1 of the 13 preinoculation cephalin cholesterol flocculation tests gave a positive reaction. The degree of flocculation was read as 2+ after forty-eight hours and this was not associated with symptoms or abnormalities in any of the other tests of liver function. With the exception of this one positive test fifty-two days prior to inoculation, no flocculation had been observed with 24 subsequent tests until that observed on the 72d day. The probability is small that a positive response to the cephalin flocculation test would occur simultaneously with abnormally increased urobilinogenuria in this subject as a result of the operation of chance. The probability of this combination occurring three times in succession as the result of chance is very much smaller. The simultaneous occurrence of abnormal results with 2 different tests of liver function has been regarded, therefore, as evidence of hepatic dysfunction.

N. M.: The liver function tests showing deviations from the normal in this subject are shown in chart 3. On the 61st day the test for urine urobilinogen was positive in a dilution of 1:60 and the test for urobilin was positive. Increased excretion of urobilinogen and urobilin continued intermittently until the 69th day. Sulfobromophthalein tests on the 61st, 63d and 65th days revealed retentions of 17, 13 and 12 per cent respectively.

With the 26 tests for urine urobilinogen performed during the 105 day preinoculation period, no reaction was obtained with urine dilutions greater than 1 to 10. The mean retention for 7 sulfobromophthalein tests was 7.2 per cent (S. D. ± 3.2; mean plus 2 S. D. — 13.6; range 2 to 11 per cent). Compared with these, the postinoculation results showed significant deviations from the normal. On the basis of the criteria cited, the occurrence of abnormal responses during the same period with two different liver function tests has been regarded as evidence of hepatic dysfunction.

E. V.: The only tests of liver function that showed deviations from the normal after inoculation were those for urine urobilinogen and urobilin. The results of the tests for urobilinogen in this subject are also shown in chart 3. With 25 tests during the 100 day preinoculation period, no reaction was obtained with urine dilutions of 1:10 or greater. On the 39th day post inoculation the test for urine urobilinogen was positive with a urine dilution of 1:30, and the test for urobilin was positive. No further abnormalities occurred until the 66th and 67th days, when the urobilinogen tests were positive with urine dilutions of 1:40 and 1:60 respectively. Increased excretions of urinary urobilinogen and urobilin continued intermittently for forty-seven days. The maximum urobilinogen excretion was represented by a positive test with the 1:75 dilution on the 98th day. The other liver function tests showed no significant abnormalities, but this person had somewhat more specific clinical symptoms, including an elevation of temperature ranging from 100 to 101.2 F. (rectal) on the 68th and 69th days, anorexia, nausea and two episodes of vomiting. Because of these symptoms and the occurrence of pathologic urobilinogenuria over a period of time corresponding to that in which hepatic dysfunction was present in 3 other members of the same group, the findings in this subject have been regarded as evidence of hepatic dysfunction.

(2) *Demonstration of Transmissible Agent in Feces of W. H., N. M. and E. V.*—Portions of feces specimens collected from these men (group P) during the first ten days after the onset of the illness produced by the "water agent" were pooled and a suspension in distilled water (pool 4 FIH) was prepared in the same manner as pool 1 FIH. Ten cc. of pool 4 FIH was administered orally to 5 previously uninoculated volunteers (group R). After fifty-four days 1 (J. B.) of the 5 men developed symptoms and signs similar to those which had been observed in the men of group P. The results of the tests which showed deviation from the normal are shown in chart 4. On the 54th day the test for urine urobilinogen was positive in a urine dilution of 1:40 and the test for urobilin was positive. Increased excretions of urobilinogen and urobilin in the urine occurred intermittently until the 66th day. The maximum excretion of urobilinogen was represented by a positive test with a urine dilution of 1 to 100 on the 66th day. The Harrison and diazo spot tests for bilirubin in the urine were positive on the 62d day only. A slight increase in sulfobromophthalein retention was found on the 58th and 61st days. On the 65th day he experienced a chill, and during the following twenty-four hours his temperature varied between 98 and 104 F. (rectal). Anorexia and pruritus were pronounced. The clinical symptoms and signs persisted for approximately a week with the exception of the temperature, which remained in the normal range after the 66th day. The other 4 men in group R have shown no significant symptoms or laboratory abnormalities during the period of six months which has elapsed. The incubation period and laboratory findings in the case of J. B. were similar, therefore, to those observed in the 4 men of group P following the ingestion of water specimen GW.

(3) *Electrophoretic Patterns of the Serum Proteins.*—Using the electrophoretic apparatus of Tiselius, studies were made on specimens of serum obtained at frequent intervals before and after the onset of hepatic dysfunction in N. M. and E. V. During the period of hepatic dysfunction, definite changes in the patterns of the serum proteins were found, and the sequence of changes was the same in the 2 cases. The sequence of changes also was the same as that observed in cases of hepatitis with jaundice produced by feces pool 1 FIH. The details of the protein alterations will be reported elsewhere.[11]

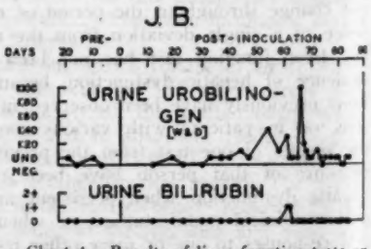

Chart 4.—Results of liver function tests on volunteer J. B. before and after inoculation with feces pool 2 FIH (specimens obtained from W. H., N. M. and E. V. during illnessea that followed ingestion of water specimen GW). See chart 2 for complete legend.

11. Chambers, L. A., and others: Electrophoretic Studies of the Serum Proteins in Hepatitis, to be published.

(4) *Testing of N. M., E. V., A. A. and J. B. for Immunity to Hepatitis Agent Excreted in Feces of Camp Patients.*—After complete recovery from the hepatic disturbances produced by the "water agent," these 4 men and 9 normal control subjects were inoculated with equivalent oral doses of feces pool 1-FIH. Seven of the 9 control subjects developed typical infectious hepatitis with overt jaundice after incubation periods of 19 to 26 days, whereas not one of the 4 men (N. M., E. V., A. A., J. B.) previously ill from the "water agent" has had symptoms of any illness during the 4 months elapsing to date. Subject E. V. showed an increased excretion of urobilinogen (chart 3) on the 24th and 38th days, but this was not associated with symptoms or abnormalities in the results of other liver function tests. Subjects N. M. (chart 3), A. A. and J. B. showed no deviations from the normal in the results of any of the liver function tests. The failure of any of these 4 men to develop definite evidence of hepatitis represents a statistically significant difference (chi square 4.01) from the results obtained in the 9 normal controls. This difference provides significant evidence that N. M., E. V., A. A. and J. B. were immune to the hepatitis agent responsible for the camp epidemic.

C. THE TRANSMISSION EXPERIMENTS

The results of the transmission experiments provide considerable information concerning the source of the camp agent and its possible methods of transmission.

The nasopharyngeal washing and urine pools contained specimens from 26 and 38 infected persons respectively. Specimens obtained both before and after the onset of hepatitis were included. If the causative agent were commonly present in the nasopharynx or urine, it should have been present in these pools. The experience with other materials make improbable the possibility that the agent, if present, was destroyed by the procedure of collection or during the period of storage. Relatively large doses were used because of the possibility that the concentration of the agent, if present, was low. That the volunteers included susceptibles is indicated by the fact that five months after inoculation with pool 2 NPIH 1 of the men was inoculated with feces pool 1 FIH and developed hepatitis with jaundice after 22 days. The evidence indicates, therefore, that the causative agent probably was not present in the nasopharyngeal washings and urine of 26 and 38 patients respectively. This, in turn, suggests that the main source of the agent at the camp was not the nasopharynx or the urine of the infected persons.

The oral transmission experiments showed that the agent was present in serum. However, parenteral injection of serum (and the Seitz filtrate of feces) known to contain the agent has not produced the disease in the 132 days that have elapsed at the time of writing. Parenterally injected blood or serum, therefore, hardly could be responsible for the large number of early cases appearing at the camp within 42 days after arrival. Since the members of the camp group could not have received blood or serum orally, the results of these experiments indicate that the majority of the camp cases were not infected after arrival by serum or blood.

The oral transmission experiments showed that a hepatitis agent was excreted in the feces of infected persons. The results in groups H and N, representing two human passages of this agent in feces, clearly show that the agent was transmissible, and the results in group L show that it passed through a Seitz filter. Furthermore, the oral administration of these materials consistently produced the disease after incubation periods of 19 to 37 days, indicating that direct or indirect transmission of the agent from feces could have been responsible for the camp epidemic.

The results in groups H, I and J compared with those in groups K and L suggest that the length of the incubation period may be influenced by the amount of the agent administered orally. Although methods of measuring the concentration of hepatitis agent in a given material have not been developed, it is known that Seitz filtrates of materials containing other viruses have a lower concentration of those viruses than the unfiltered materials.[12] It is probable, therefore, that the 2 cc. dosage of the Seitz filtrate of pool 1 FIH (group L) contained a smaller amount of the hepatitis agent than the quantities of the unfiltered material given to groups H, I and J. It also seems reasonably certain that the men of group K received a smaller amount of the hepatitis agent than did the men in groups H, I and J. The mean incubation period for the combined groups H, I and J (11 cases) was 21.5 days and the longest incubation period was 26 days. For the combined groups K and L (5 cases) the mean incubation period was 32 days and the shortest incubation period was 28 days. The absence of any significant differences in the severity of the illnesses of the men in groups H, I and J as compared with those of the men in group L affords some evidence that the longer incubation periods in the men of group L probably were due to smaller doses of the agent rather than to a change in its virulence resulting from the filtration process. However, the illnesses in the men of group K were much milder than those of the men in groups H, I, J and L, suggesting that the virulence, as well as the concentration, of the agent received by group K may have been decreased by the treatment to which it was subjected. Although these groups are too small for the results to be conclusive, the available evidence suggests that the length of the incubation period may be related inversely to the quantity of ingested hepatitis agent and possibly to its virulence.

As previously stated, the water from the girls' well showed bacteriologic evidence of fecal contamination. Since the hepatitis agent was excreted in feces, the contamination of this water with feces strongly suggests that water may have been the means of transmission of the agent at the camp. However, the occurrence, after the usual incubation period, of hepatitis in human volunteers following the ingestion of this water under controlled conditions would constitute the only conclusive proof that the water contained the hepatitis agent. For this reason the conclusions regarding the method of transmission of the agent at the camp depend to a considerable extent on the interpretation of the results obtained by the administration of water specimen GW to volunteers (group P). The occurrence of illnesses associated with hepatic dysfunction in 4 of the 5 men at nearly the same time after ingestion of this water and the absence of any similar disturbance among control subjects living under the same conditions definitely relate the illnesses in these men to the one variable, namely the ingestion of water specimen GW. The individual liver function tests giving abnormal results in this group of men during their illnesses included those for urine urobilinogen, urine urobilin, urine bilirubin, serum bilirubin, qualitative

12. Henle, W.: Personal communication to the authors.

van den Bergh reaction, cephalin cholesterol flocculation and sulfobromophthalein excretion. Abnormal results with this group of tests can be regarded as unquestionable evidence of hepatic dysfunction, regardless of the cause. The demonstration of the presence of an agent capable of producing the same illness when administered to other volunteers (group R) in the feces of these men indicated that the illnesses were due to a transmissible agent. Since the chances of isolating two different transmissible agents that produced hepatic dysfunction, one from the feces of the camp patients and the other from the camp water supply, would be extremely small, it is logical to assume that the "water agents" and the "feces agent" were the same. This assumption is supported by: (*a*) The electrophoretic studies, which showed that the illness produced by the "water agent" and the hepatitis produced by the "feces agent" were associated with the same sequence of changes in the serum proteins.[13] The significance of the sequence of changes occurring in the serum proteins during hepatitis has not yet been established. However, in 5 cases (with jaundice) studied to date the sequence of changes has been the same and thus appears to be a characteristic occurrence in hepatitis. Whether the same sequence of changes occurs in other diseases is not known, so that these findings cannot be regarded as characteristic only of hepatitis. (*b*) The experimental evidence showing that N. M., E. V., A. A. and J. B., after recovery from the hepatic disturbances produced by the "water agent," were immune to the "feces agent."

TABLE 4.—*Incubation Periods in Persons with Limited Periods of Exposure*

Case	Exposure: Date or Dates	Exposure: Duration	Exposure: Place	Date of Onset	Incubation Period: Minimum	Incubation Period: Maximum
A	7/27/44	2 hours	Camp	9/ 2/44	37	37
B	7/27/44	12 hours	Camp	8/12/44	34	34
C	7/29/44	12 hours ±	Camp	8/28/44	30	30
D	8/3 to 8/8/44	5 days	Camp	9/ 2/44	25	30
E	7/9 to 7/19/44	8 days	Camp	8/12/44	26	34
2	6/30 to 7/7/44	8 days	Camp	7/24/44	20	28
F	8/25 to 9/2/44	8 days	Philadelphia	10/ 3/44	31	39
G	8/7 to 8/13/44	7 days	Hospital	8/21/44	8	14

However, the illness produced in the men of groups P and R by the "water agent" differed from that produced by the agent in the feces of the camp patients in the following two ways: (*a*) None of the 5 men developed overt jaundice; (*b*) the incubation periods ranged from 54 to 71 days. The fact that hepatitis may occur without jaundice is now well established. The ratio of cases with jaundice to those without jaundice apparently varies in different epidemics from approximately 2.7 to 1 as observed in this epidemic to estimates of 1 to 2 or more in Italy.[17] Thus the failure of the men in groups P and R to develop overt jaundice does not constitute evidence that they did not have hepatitis. However, if the "water agent" was the same as the "feces agent," at least 1 of the 5 men might have been expected to develop overt icterus unless a decrease in virulence of the agent had occurred. At the time of collection of water specimen GW, no water had been pumped from the well for at least 5 weeks and the camp had been closed for 8½ weeks. The water specimen then was stored in a laboratory at room temperature in plain glass water bottles, unprotected from light, for another month before it was administered to group P. These conditions could have resulted in attenuation of the hepatitis agent. In addition, it is reasonable to assume that the concentration of the agent in this water probably was low, and the results of the transmission experiments in groups H, I and J, and in groups K and L have indicated that the length of the incubation period may vary inversely with the amount of the agent ingested. Additional evidence that the quantity of virus administered to human beings may influence the length of the incubation period is provided by the recent report of the Commission on Acute Respiratory Diseases.[18] The investigators found that the incubation period of primary atypical pneumonia produced experimentally in volunteers by the administration of a filtered material was approximately one week longer than that following the administration of the same amount of this material prior to the filtration. The longer incubation periods and the mildness of the disease observed in groups P and R could be explained, therefore, by a low concentration of attenuated virus.

D. CONCLUSIONS BASED ON TRANSMISSION EXPERIMENTS

1. The main source of the hepatitis agent at the camp probably was the feces of infected persons.

2. The agent in feces was transmissible to human beings.

3. The agent in feces passed through a Seitz filter.

4. The evidence indicates that water from the girls' well contained a hepatitis agent which probably was the same as that excreted in the feces of the camp patients.

5. The agent probably was present in the blood of infected persons at some stage of the disease.

6. Nasopharyngeal droplets or secretions and urine probably were not common sources of the agent at the camp.

III. EPIDEMIOLOGIC OBSERVATIONS

In this report, only the factors related to the sources of the agent and its method or methods of transmission at the camp will be considered.

A. INCUBATION PERIOD

The most satisfactory data on the length of the incubation period are those pertaining to a few persons who had a more limited period of exposure than the members of the camp group (table 4). In 3 persons who visited the camp for only 2 to 12 hours on 1 day (patients A, B and C) the incubation periods were 30, 34 and 37 days. In 2 who visited for 5 and 8 days (patients D and E), the minimum periods were 25 and 26 days and the maximum were 30 and 34 days respectively. The female counselor (patient 2) who was exposed to the initial case for the first 7 days

13. The changes in the various protein components demonstrated by the electrophoretic method were not shown by quantitative chemical determinations on the same specimens.

Footnotes 14, 15 and 16 deleted on proof.

17. Barker, M. H.: Personal communication to the authors.

18. Commission on Acute Respiratory Diseases: Transmission of Primary Atypical Pneumonia to Human Volunteers, J. A. M. A. **127**: 146 (Jan. 20) 1945.

developed the disease after a minimum period of 20 and a maximum period of 28 days. After a boy camper had returned to his home, his cousin (patient F) visited him in his home for a week and left the day before he developed the initial symptoms of hepatitis. Case F developed the disease after a minimum period of 31 and a maximum incubation period of 39 days. The shortest incubation period apparently was that of a hospital nurse (patient G) who was never at camp but who constantly attended a boy camper for 7 days during the preicteric period of his illness. Her first symptoms occurred after a minimum period of 8 and a maximum period of 14 days. However, overt jaundice did not appear for 24 days after her first symptoms. Finally, 53 persons (chart 1) developed the disease during the 6th week of the camp season. Since it is unlikely that these persons were all infected immediately on arrival, the incubation periods were probably less than 42 days. Thus the possible range of the incubation periods in these 61 cases of hepatitis was 8 to 42 days, and in 3 of those in which exposure was limited to 1 day it was 30 to 37 days.

The incubation periods observed in volunteers experimentally infected with feces pool 1 FIH (specimens obtained from camp group) ranged from 19 to 37 days, thereby substantiating the foregoing observations.

These data on incubation periods, those reported by others [19] and the evidence of infection of visitors to the camp provide support for the basic assumption necessary for a discussion of the method or methods of transmission, namely that the majority of the camp group acquired the infection after arrival at camp. This assumption is supported by the fact that many of those involved early were from different cities and towns. Their nearly simultaneous infection with a hepatitis agent by natural means before coming to the camp would therefore be almost impossible. The data on incubation periods also indicate that patient 1, who developed hepatitis only 3 days after arrival, was infected elsewhere.

B. SOURCE OF HEPATITIS AGENT

Since hepatitis had not occurred at this camp in previous years and no other source of the agent has been detected, it is reasonable to assume that it originated from patient 1, who developed the disease 3 days after the opening of the camp. This is supported by the following facts: (1) the second person (patient 2) to develop the disease lived in the same cabin (A) and was therefore closely exposed to case 1 before and after the onset of hepatitis; (2) in relation to the time of onset in case 1, the epidemic began after an interval of time that is compatible with the observed length of the incubation period of the disease.

The source of the infection of patient 1 is unknown. She had had no recognized exposure to patients with hepatitis and no injection of a homologous blood product.

C. CHARACTERISTICS OF THE EPIDEMIC

As shown in chart 1, the early cases occurred predominantly in the female group. The first 2 persons (patients 1 and 2) to develop the disease lived in the same cabin (A). The onset in case 1 was on the 3d day of the season and in case 2 the disease developed 24 days later but approximately 10 days before the explosive appearance of the epidemic. This suggests that patient 2 was infected earlier and possibly by a different method than the others. However, the 40 persons in the female group who developed signs of the disease during the 6th week were quartered in a number of different cabins and had no unusual exposure to the earlier cases. In fact, as patient 1 was confined to cabin A from the 4th to the 6th day and to the girls' infirmary from the 7th to the 10th day and left for her home on the 11th day, the period during which the female group as a whole could have been exposed to her was limited to the first 3 days. Furthermore, the 13 persons in the male group who developed hepatitis during the 6th week also lived in different cabins and included young campers who would have had little or no chance of being exposed to the early cases in the female group. Thus, a relatively large number of the female group and a small number of the male group apparently were infected at nearly the same time by some method that did not require personal contact. Furthermore, the low incidence of secondary cases previously mentioned indicates that the agent was not easily transmitted to contacts. The data on the incubation period of the disease show that it did not exceed 42 days in the 61 cases on which satisfactory data are available. Thus, the fact that the disease continued to appear in members of the camp group over a period of at least 70 days suggests that, although a number of persons in both the male and female groups were probably infected at nearly the same time, others were probably infected at different times. This is indicated also by the facts that the majority of the cases in the female group occurred earlier than the majority in the male group and the incidence curves in both groups showed two distinct peaks (chart 1). For these reasons a source of infection must have been present over a period of time. The occurrence of hepatitis in persons who arrived at or visited camp during the 2d, 4th, 5th and 6th weeks indicates that a source of infection was present for at least the first 6 weeks.

Thus, the chief epidemiologic characteristics requiring explanation are (1) the unusually high incidence of the disease in the entire camp group, which appears to be the highest that has been reported in any group in this country during a similar period of time; (2) the higher total incidence in the female than in the male group; (3) the predominance of the early cases in the female group and the later cases in the male group; (4) the simultaneous infection of a number of persons at the camp who had not been in close personal contact; (5) the infection of others after a longer period of residence at the camp; (6) the apparent ease with which the infectious agent was acquired at the camp in contrast to the apparent lack of ease with which it was acquired by those in contact with infected persons away from the camp.

D. POSSIBLE METHODS OF TRANSMISSION OF THE CAUSATIVE AGENT

In order to obtain a satisfactory explanation for the described characteristics of the epidemic, the various methods by which the infectious agent might have been transmitted at the camp have been investigated. The evidence for and against these methods, as provided

19. Epidemic Infective Hepatitis, editorial, Brit. M. J. **2**: 680 (Nov. 27) 1943. Ford, J. C.: Infective Hepatitis, Lancet **1**: 675 (May 29) 1943.

by the observations made at the camp and by the results of the transmission experiments in volunteers, is as follows:

Transmission by Air.—The members of the camp group lived in cabins accommodating 7 to 10 campers and 1 to 2 counselors. Circulation of air in and out of cabins was free. Beds were approximately 3 feet apart. The entire male and female groups ate at one time in their respective dining rooms, each of which consisted of a single large airy room with many small tables accommodating 10 to 12 persons. Thus there was ample opportunity for transmission of an infectious agent by air. However, the explosive type of the onset of the epidemic, the infection soon after arrival at camp of some persons in the male group who had not been in close personal contact with the female group, the lack of ease with which the agent was acquired away from the camp and the failure of nasopharyngeal washings to produce the disease in volunteers all indicate that the majority of persons were not infected by an air borne agent.

Transmission by Fomites.—Because of the well known tendency of young persons to use articles in common, spread of the infectious agent by this means would have been quite possible in groups such as these. Undoubtedly certain articles in the cabins were used by several or all of the residents. Dishes and eating utensils were washed by hand, rinsed in hot water and then in a germicidal solution (Roccol-Winthrop Chemical Company). However, the care with which this procedure was carried out was subject to individual variation and, in view of the known resistance of the hepatitis agent to some methods which destroy bacteria, the agent might have survived the cleansing process. For these reasons, transmission by fomites may have been the method responsible for the infection of some persons at the camp and also for the 5 persons who had not been at the camp. However, the same observations cited under transmission by air indicate that fomites probably were not responsible for transmitting the agent to the majority of the persons at the camp.

Transmission by Biting Insects.—Since extremely small amounts of serum injected parenterally have transmitted a hepatitis agent to volunteers [20] and evidence has been obtained that suggests transmission by the minute amounts of serum remaining in improperly sterilized syringes and needles,[21] it might be possible for biting insects to transmit mechanically the agent in blood from one person to another. Since "stable flies," "deer flies" and mosquitoes were unusually abundant at the camp from the beginning of the season, there would have been ample opportunity for this type of transmission. However, parenteral injection of a pooled serum and a Seitz filtrate of feces (both known to contain the camp hepatitis agent) into previously uninoculated volunteers (groups C and M) has not resulted in hepatitis in the 132 days that have elapsed to date. This provides reasonable evidence that the many persons developing hepatitis within 40 days after arrival at the camp were not infected from blood carried by biting insects. This method, therefore, probably was not responsible for transmitting the agent to the majority of the cases, although it cannot be eliminated as a possible means of infection of some persons who developed the disease in the later weeks of the epidemic. One other observation also suggests that the agent was not transmitted by biting insects. A number of persons spent varying amounts of time during the camp season at a small boarding house located adjacent to the camp. The distance between this boarding house and the girls' section was no greater than that between the midpoints of the boys' and girls' sections. The source of water for the boarding house was different from that of the camp. Questionnaires were sent to 42 persons who had not visited at the camp but had resided at the boarding house during the camp season. None had subsequently developed hepatitis. If the agent had been transmitted by biting insects, it would seem that some of these persons also would have been infected.

Direct Transmission from Person to Person.—Ample opportunities for this method of spread obviously would be present in groups such as those at the camp. Although some persons may have been infected in this way, direct transmission would not account for the explosive type of onset of the epidemic, involving persons, in both the female and male groups, who apparently had not been in close personal contact with other infected persons. It is unlikely, therefore, that direct transmission of the infectious agent from person to person was responsible for the majority of the camp cases.

The evidence cited has indicated that in the majority of the early cases at the camp infection probably did not occur by an agent transmitted directly from person to person, or indirectly by air, fomites or biting insects. The explosive type of onset of the epidemic suggests that a large number of persons were infected at approximately the same time. This indicates that the infectious agent was acquired from a common source to which a large number of persons were exposed at nearly the same time. In epidemics of other diseases which have been characterized by an explosive onset a common source of infection usually has been found, and the source usually has been contaminated food, milk, water or other materials which had been ingested by, or injected into, a number of persons within a short period of time. Since the members of the camp group had not been injected with any material before or after arrival, food, milk or water remained as possible sources of infection.

Transmission by Food.—The camp food supplies were procured from outside sources and were delivered to the boys' camp. The food supplies for the girls' section were obtained from the storeroom in the boys' section and all food, with the exception of pastries and desserts, was prepared and cooked by different personnel in the respective kitchens of the two sections. Pastries and desserts were prepared in the "boys' kitchen" and sent to the girls' section. Thus food was sent from the boys' to the girls' section, but no food was transferred from the girls' to the boys' section. Since the epidemic originated in the girls' section and no food was sent from there to the boys' section, the early cases in the boys' section could not have been caused by a food borne agent. It is also improbable that infection in the early cases in the female group were caused by a food borne agent for the following reasons: (*a*) none of the early cases in the girls' section had had any contact with food supplies, and eating utensils contaminated by those involved were not a probable means of infection of the majority of cases for reasons previously discussed; (*b*) none of the food handlers were among the early cases of hepatitis and none had had the disease previously, at least not in a recognizable form; (*c*) none of the cooks, all of whom were in the older age group, developed the disease before or after the onset of the epidemic; (*d*) the persons involved in the explosive onset of the epidemic, although predominantly females, also included a number of the male group; (*e*) contamination of food in both sections with an infectious agent carried by insects was not likely because insects had little or no access to feces which the transmission experiments have indicated was the probable source of the infectious agent; (*f*) several persons who visited the camp for only a few hours on one or more days, but did not eat there, subsequently developed hepatitis. These observations indicate that food probably was not the carrier responsible for transmission of the agent to the persons involved in the early phases of the epidemic.

Transmission by Milk.—All milk was obtained from the same dairy and was delivered to the kitchens of both sections of the camp. If the milk had been contaminated prior to arrival at the camp, the outbreak of the disease should have occurred simultaneously in the two sections. Also other camps in the

20. Oliphant, J. W.; Gilliam, A. G., and Larson, C. L.: Jaundice Following Administration of Human Serum, Pub. Health Rep. **58**: 1233 (Aug. 13) 1943. Oliphant, J. W.: Jaundice Following Administration of Human Serum (Harvey Lecture), Bull. New York Acad. Med. **20**: 429 (Aug.) 1944.

21. Salaman, M. H.; King, A. J.; Williams, D. I., and Nicol, C. S.: Prevention of Jaundice Resulting from Antisyphilitic Treatment, Lancet **2**: 7 (July 1) 1944. Sheehan, H. L.: Epidemiology of Infective Hepatitis, ibid. **2**: 8 (July 1) 1944.

vicinity, using the milk from the same dairy, had no cases of hepatitis. These observations justify the exclusion of milk, contaminated prior to arrival at the camp, as a source of the infectious agent. That milk contaminated after arrival at the camp probably was not the source of infection in the early cases is indicated by the observations relating to food as described.

Transmission by Lake Water.—During the camp season, nearly every one bathed in the camp lake at one time or another. This lake was used only by the camp group and was fed by streams which were not subject to any known source of contamination. Since many persons bathed in this lake prior to the onset of the epidemic, it is possible that the water might have been contaminated with the hepatitis agent from them, resulting in the infection of some persons. However, patient 1 did not bathe in the lake because of the onset of her illness 3 days after arrival. Furthermore, a few persons who did not bathe in the lake developed the disease in the early phases of the epidemic. Finally, several persons who visited the camp for only a few hours on one day and did not go into the lake subsequently developed hepatitis. Thus, it is not likely that, in the early cases at least, the infection was acquired from the lake water.

Since food, milk and the lake water apparently would not account for some of the main features of the epidemic, drinking water alone remained a possible source of the infection.

Transmission by Drinking Water.—The water used for drinking and washing purposes at the camp all came from two driven wells, one (approximately 220 feet deep) located in the girls' section and the other (approximately 190 feet deep) located in the boys' section. The girls' section was supplied entirely by water pumped directly from their well into the lines or from their reservoir located adjacent to the well. However, the supply from the boys' well was often inadequate and therefore was supplemented frequently by water pumped directly from the girls' well to a reservoir located in the boys' section. Thus the water used by the female group came only from their well, whereas that used by the male group came from both wells. Water from the girls' well first was pumped into the boys' reservoir during the first week of the season and thereafter was pumped into this reservoir at frequent intervals until the camp was closed. Thus contamination of the water from the boys' well with the hepatitis agent would not account for the epidemiologic phenomena. However, contamination of the water in the girls' well would satisfactorily explain (*a*) the higher total incidence in the female than in the male group; (*b*) the predominance of the early cases in the female group and the later cases in the male group; (*c*) the infection of a number of persons in both groups soon after their arrival at camp; (*d*) the persistence of a source of infection during at least the first 6 weeks; (*e*) the apparent ease with which the agent was acquired at the camp in contrast to the apparent lack of ease with which it was acquired away from the camp; (*f*) the unusually high incidence of the disease in the entire group within a period of 7 weeks.

In addition, continuous, and possibly increasing, contamination of the water in the girls' well with the hepatitis agent would provide an explanation for the two peaks in the weekly incidence curves of both groups (chart 1). Sufficient amounts of agent could have been provided by the feces of patients 1 and 2 to account for the early infection of a considerable number of persons in the female section where the well water was not "diluted" with water from other sources. In the male section, most of the water was provided by their own well, the proportion contributed by the girls' well being relatively small. This would explain the occurrence of only a few cases in the boys' section during the week in which the highest incidence was observed in the girls' section. Continued contamination of the boys' water with that from the girls' well would result in the eventual infection of a sufficient number of persons to explain the first peak in the male epidemic curve. The delayed secondary peaks in both groups would be best explained, however, by not only continuous, but also increasing, contamination of the water. An increased contamination would have been most apt to occur when the early cases in the female section were admitted to the infirmary (see Sources of Contamination of Girls' Well Water). This explanation is supported by the fact that the two peaks in the incidence curves of both groups were separated by an interval of 4 weeks, which is equivalent to the length of the incubation period. The lower height of the secondary peak in the female group as compared with that in the male group might be explained by the facts that (*a*) the chance of acquiring the agent early was greater in the female section and the number of female susceptibles, therefore, was reduced more rapidly, (*b*) the length of the period during which the agent might have been acquired was shorter as a result of the earlier closure of this section, and (*c*) the total number of persons in the group was smaller. Although the secondary peaks can be explained satisfactorily on the basis of continued, and possibly increasing, contamination of the water, the large number of early cases also provided increasing opportunities for acquiring the agent from sources other than water. The interval between the primary and secondary peaks also supports this possibility. On the other hand, the apparent lack of easy transmissibility of the agent, as observed away from the camp, suggests that the sources other than water probably were not, by themselves, responsible for the secondary peaks. It is quite possible, however, that these sources contributed to the height of these peaks.

From the evidence cited to date, transmission by water from the girls' well appears to be the only method which, on theoretical grounds alone, could satisfactorily explain the chief characteristics of this epidemic. The theoretical explanation has been substantiated by the following facts: (*a*) The transmission experiments showed that the causative agent was excreted in feces; (*b*) the water from the girls' well showed bacteriologic evidence of fecal contamination on two different occasions; (*c*) the transmission experiments provided evidence that water from this well contained a transmissible agent that produced in volunteers an illness associated with hepatic dysfunction and an immunity to the agent excreted in the feces of the camp patients. The combined results of the epidemiologic and bacteriologic studies and the transmission experiments in volunteers have led to the conclusion that the infectious agent was transmitted to the majority of the camp cases by water from the girls' well.

Possible Sources of Contamination of Water from Girls' Well.—On the basis of the foregoing conclusion, attempts were made to locate a source of contamination of the water from the girls' well. The toilets were of a type that would not permit "back flow" of fecal material into the water lines. The water reservoir was covered and was not subject to contamination except from the entering water. The well was covered at its surface, and contamination could not have entered from above. A search for leaks in the pipe lines revealed none. For these reasons the contaminating material probably entered the well below its surface. The only apparent sources of contaminating material were a number of cesspools located within a radius of 200 feet from the well. These cesspools were 6 to 8 feet in depth and had open bottoms, stone walls and cement tops. Each cesspool received the sewage and waste water from one to three cabins. None of the cesspools had overflowed prior to the start of the epidemic. In fact, although in use for a number of years, drainage of the cesspools had never been necessary, indicating that the contents had diffused into the ground. The ground layer of the area, varying in depth from a few inches to approximately 4 or 6 feet, consisted of ordinary top soil overlying a layer of "hardpan." The exact nature of the underlying rock was not determined, but it was said to consist of red shale and limestone. In certain places where the rock layer protruded through the soil and could be inspected, many cracks and fissures were apparent.

As shown in chart 5, the girls' well was nearly surrounded by cesspools. The sewage from cabins C and D was received by cesspools 3 and 4, located 200 and 100 feet respectively from the well. None of the persons living in these cabins were among the earliest to acquire hepatitis. However, cesspool 1,

located 150 feet from the well, received all the sewage from cabin A and the girls' infirmary. As mentioned previously, patient 1, who developed hepatitis 3 days after the opening of the camp, and patient 2, who developed hepatitis 27 days after the opening of the camp and approximately 1 week before the onset of the epidemic, both lived in cabin A. Furthermore, most of the early cases of hepatitis were "hospitalized" in the girls' infirmary. Thus cesspool 1 probably received feces containing the hepatitis agent almost continuously after the opening day of camp. Since the girls' well water must have been contaminated with the hepatitis agent soon after the opening of the camp to result in the explosive onset of the epidemic during the 6th week, and cesspool 1 was the only one relatively certain to have contained the hepatitis agent during the first few weeks, it is highly probable that cesspool 1 was the source of contamination. Another possible source of the hepatitis agent after the 6th week would have been cesspool 2, located only 75 feet from the well. This pool received sewage from the girls' lodge. Prior to the epidemic, the lodge was used only on the infrequent rainy days. In the 6th and 7th weeks, however, the number of cases of hepatitis exceeded the capacity of the girls' infirmary, and during that period approximately 45 hepatitis patients were quartered in the lodge. Thus during and after the 6th week either or both cesspool 1 and 2 could have provided increasing amounts of the hepatitis agent.

Unfortunately the probable relationship between the epidemic and cesspool 1 (and possibly cesspool 2) did not become apparent until the analysis of the epidemiologic data had been completed (November 1944). By that time the contamination of the well water had ceased,[22] possibly because of the lack of use of the cesspools after August 20. Thus the opportunity of obtaining additional evidence of a connection between the well and the cesspools was missed.

Chart 5.—Approximate location of cesspools in relation to well in girls' section of camp. Well is indicated by circle at point of convergence of arrows. Cesspools are indicated by numbered squares. Numbers on arrows represent approximate distance in feet from cesspools to well. Cesspool 1 received the sewage from cabin A and the female infirmary. Cesspools 2, 3 and 4 received the sewage from cabin B, the female lodge and cabin C respectively (see text).

The epidemiologic observations and the results of the experimental studies have led to the following conception of the pathogenesis of this epidemic: The hepatitis agent was brought into the camp on the first day of the season by patient 1. By means of a connection between cesspool 1 and the well in the girls' section, the water supply was contaminated with this agent. The majority of persons in both groups and some visitors probably acquired the agent from the water. Some persons may have acquired the agent (*a*) from feces, directly or indirectly; (*b*) possibly from blood carried by biting insects.

IV. COMMENT

On the basis of the epidemiologic observations alone, water from the girls' well appeared to be the only means of transmission of the hepatitis agent at the camp which could satisfactorily account for the chief characteristics of this epidemic. The transmission experments showed that the hepatitis agent was excreted in feces, and the bacteriologic studies provided evidence of fecal contamination of the girls' well water. Finally, the transmission experiments provided experimental evidence that this water contained a transmissible agent which probably was the same as that excreted in the feces of the camp patients. It is possible that the agent was transmitted to some persons at the camp (*a*) directly from infected persons, (*b*) indirectly by contaminated fomites or lake water and (*c*) in blood carried by biting insects. However, the data provided by the epidemiologic observations, the bacteriologic studies and the transmission experiments in volunteers all lead to the conclusion that the hepatitis agent was transmitted to the majority of the camp cases by water from the girls' well.

The evidence presented herein of the excretion of the hepatitis agent in the feces of patients with the disease confirms that previously reported by others.[23] It seems certain, therefore, that feces is the source of the agent responsible for many epidemics of infectious hepatitis and that anything subject to contamination with feces is a potential means of transmission of this disease.

The results of this investigation suggest that the agents responsible for some of the past epidemics of infectious hepatitis may have been water borne. Fraser[24] and Hallgren[25] have reported epidemics of infectious hepatitis in which transmission by water was suspected because of bacteriologic evidence of fecal contamination. However, the epidemic reported herein appears to be the first epidemic of infectious hepatitis in which experimental evidence of the method of transmission has been obtained.

It is apparent that the prevention of future epidemics of hepatitis may depend in part on the control of the agent (or agents) in water. In view of the known resistance of this agent to procedures which usually eliminate or destroy bacteria,[26] the effect of the current methods of water disinfection on this agent becomes a question of importance. Evidence recently has been obtained that the agent of infectious (epidemic) hepatitis in contaminated water was not inactivated by treatment of the water with sufficient chlorine to provide a residual concentration of 1 part per million after 30 minutes' contact. It also may have survived, in a much attenuated form, the treatment of contaminated water with sufficient chlorine to provide a residual concentration of 15 parts per million after 30 minutes' contact.[10] It is probable, therefore, that special measures, yet to be determined, will be required to eliminate the hazard of transmission of this agent by water.

The outbreak of "gastrointestinal upsets" that occurred in the camp group 1 to 3 weeks prior to the onset of the epidemic of acute hepatitis is of interest. It is possible that these manifestations were entirely unrelated to the epidemic disease. However, it seems probable that some relationship existed. If so, they may have been due to an agent, other than the hepatitis agent, that also was present in the water as a result of fecal contamination. On the other hand, it is possible that these symptoms and signs represented the first manifestations of the hepatitis agent. A number of the group who developed hepatitis 3 to 4 weeks after returning home reported similar transient upsets 1 to 3 weeks prior to the abrupt onset of acute hepatitis. Furthermore, 3 of the volunteers inoculated with feces pool 1 FIH had similar transient episodes 1 to 2 weeks before the onset of acute hepatitis. One of the 3 had

22. Bacteriologic examination of water obtained from the girls' well on Nov. 28, 1944 and of 3 specimens obtained during March and April 1945 showed no evidence of contamination.

23. MacCallum, F. O., and Bradley, W. H.: Transmission of Infective Hepatitis to Human Volunteers, Lancet **2**: 228 (Aug. 12) 1944. Havens, W. P., Jr.; Ward, R.; Drill, V. A., and Paul, J. R.: Experimental Production of Hepatitis by Feeding Icterogenic Materials, Proc. Soc. Exper. Biol. & Med. **57**: 206 (Nov.) 1944.

24. Fraser, R.: A Study of Epidemic Catarrhal Jaundice, Canad. Pub. Health J. **22**: 396, 1931.

25. Hallgren, R.: Acta med. Scandinav., Supp. 140, 1942.

26. Havens, W. P., Jr.: Properties of the Etiologic Agent of Infectious Hepatitis, Proc. Soc. Exper. Biol. & Med. **58**: 203 (March) 1945. MacCallum and Bradley.[23]

bilirubinuria for 2 days during that period. In a previous report, evidences of the occurrence of transient symptoms and signs associated with mild hepatic dysfunction 1 to 3 months prior to the onset of acute homologous serum hepatitis has been presented.[4] These observations suggest that the "gastrointestinal upsets" observed at the camp prior to the epidemic of hepatitis may have been the first manifestations of the disease.

V. SUMMARY

During the late summer of 1944 an epidemic of infectious hepatitis occurred in a large summer camp for boys and girls. Three hundred and fifty of 572 persons developed hepatitis within a period of 13 weeks. The onset of the disease in 344 of the 350 patients was within a period of 7 weeks. This appears to be the highest recorded incidence of this disease in any group in this country over a similar period of time. Of the 350 patients with hepatitis 255 had overt jaundice and the remaining 95 had the nonicteric form of the disease. At least 9 persons who visited the camp for short periods during the first 6 weeks of the season subsequently developed hepatitis. Approximately 175 persons returned to their homes after the onset of hepatitis at the camp, and approximately 175 others developed the disease as late as 5 weeks after their return home. Among the many friends and relatives who had not visited the camp but subsequently were exposed at home to infected persons from the camp, only 5 secondary cases have been reported. No deaths occurred.

The outstanding characteristics of the epidemic were (1) the unusually high incidence of the disease, (2) the higher total incidence in the female than in the male group, (3) the predominance of the the early cases in the female group and of the later cases in the male group, (4) the simultaneous infection of a number of persons at the camp who had not been in personal contact with one another and (5) the apparent ease with which the infectious agent was acquired at the camp in contrast to the apparent lack of ease with which it was acquired by those in contact with infected persons away from the camp.

In order to determine the source of the causative agent and the method or methods of transmission at the camp, an epidemiologic survey was made and human volunteers were inoculated with serum, nasopharyngeal washings, urine and feces collected from the camp patients, and with water, and a preparation made from flies, obtained at the camp.

The transmission experiments in volunteers provided the following information concerning the source of the agent and its methods of transmission: (1) Nasopharyngeal droplets or secretions and urine probably were not common sources of the agent because of the failure of these materials to produce the disease in volunteers; (2) the agent was present in the blood and feces of infected persons; the agent in these materials produced the disease in volunteers, indicating that it was transmissible; (3) serum produced the disease in human volunteers after an incubation period similar to that observed at the camp only when given by the oral route; normal volunteers injected parenterally with the same serum have not developed hepatitis during the 132 days which have elapsed to date; (4) the chief source of the agent at the camp probably was the feces of infected persons; (5) a preparation made from flies trapped at the camp did not produce the disease in volunteers, suggesting that these flies were not carrying the caustive agent; (6) the production of the disease in volunteers by a filtrate obtained by the passage of feces through a Seitz filter indicated that the agent was filtrable; (7) a decrease in the quantity of the agent administered orally apparently resulted in an increase in the length of the incubation period; (8) water from one of the camp wells (female section) produced in 4 of 5 volunteers a mild illness associated with hepatic dysfunction. These illnesses and hepatitis produced in other volunteers by the "feces agent" were associated with the same sequence of changes in the electrophoretic patterns of the serum proteins. A second human passage of the "water agent" was accomplished by the administration to other volunteers of feces obtained from the men infected with the "water agent." After recovery from their infection with the "water agent" the 4 men tested showed evidence of immunity to the "feces agent."

The epidemiologic observations and the results of the transmisison experiments provided evidence that the causative agent probably was not transmitted to the majority of the persons at the camp by air, fomites, biting insects, food, milk, the lake water or directly from infected persons. On the basis of the epidemiologic observations alone, water from the well in the girls' section appeared to be the only potential carrier of the infectious agent that could satisfactorily explain the outstanding characteristics of the epidemic. The transmission experiments showed that the hepatitis agent was excreted in feces, and the bacteriologic studies provided evidence of fecal contamination of the girls' well water. Finally, the transmission experiments provided experimental evidence that this water contained a transmissible agent which was probably the same as that excreted in the feces of the camp patients. The data provided by the epidemiologic observations, the bacteriologic studies and the transmission experiments in volunteers all lead to the conclusion that the infectious agent was transmitted to the majority of the cases at the camp by water from the girls' well. The source from which the well water was contaminated with the hepatitis agent was not demonstrated, but the available evidence indicates that the source was a cesspool, located near the well, which received the excreta from 1 or more infected persons almost continuously after the first day of the camp season.

CONCLUSIONS

1. The evidence indicates that the agent responsible for this epidemic was water borne.

2. The causative agent of infectious hepatitis is excreted in the feces of persons with the disease. The evidence presented herein confirms the observations of others in this respect.

3. Anything subject to direct or indirect contamination with feces provides a potential means of transmission of this disease.

4. This appears to be the first epidemic of infectious hepatitis (not homologous serum hepatitis) in which experimental evidence of the method of transmission has been obtained. As far as known, this also appears to be the first satisfactory evidence of the natural transmission to man of any virus agent by water.

DISINFECTION OF WATER CONTAINING CAUSATIVE AGENT OF INFECTIOUS (EPIDEMIC) HEPATITIS

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During the past few years the incidence of infectious (epidemic) hepatitis has increased to such an extent that the disease has become one of the most serious medical problems of the present war. The development of effective methods for its prevention and control has been prevented by the lack of definite knowledge concerning the sources of the causative agent and the factors involved in its transmission. However, recent investigations[1] have shown that the causative agent is excreted in the feces of infected persons. This has suggested that feces may be a common source of the agent and that anything subject to fecal contamination may be a potential means of transmission of the disease. More recently, evidence has been obtained that the agent from feces may be transmitted by drinking water.[2] It has seemed important, therefore, to determine the effect on the hepatitis agent of methods commonly used for the disinfection of drinking water. For this reason, an initial experiment concerned with the effect on the hepatitis agent of a concentration of chlorine commonly used for the emergency disinfection of drinking water was conducted. Because the results showed that the hepatitis agent was not destroyed by this treatment, the effect of a higher concentration of chlorine was tested. Also an attempt was made to remove the agent from contaminated water by coagulation and adsorption with sodium carbonate, aluminum sulfate and activated carbon. The present report deals with the methods and results of these investigations.

MATERIALS

EXPERIMENT A (*Effect of Chlorination*).—Ten cc. of a 10 per cent feces suspension (pool 1 FIH), known to contain the agent of infectious hepatitis and described in detail elsewhere,[2] was added to each of two bottles (water specimens 1 and 2) containing 18,000 cc. of distilled water. Each water specimen thus contained approximately 55 parts of feces per million parts of water.

1. Water Specimen 1: This water was not subjected to further treatment.

2. Water Specimen 2: This was treated with chlorine in accordance with a technic commonly used for the rapid disinfection of drinking water under emergency conditions. The technic requires the addition of sufficient chlorine to provide a residual chlorine concentration of 1 part per million after a contact period of thirty minutes. The procedure was carried out as follows:

The chlorine demand of the contaminated water was determined by testing a number of portions for residual chlorine (starch-potassium iodide method; titration with sodium thiosulfate) thirty minutes after the addition of varying amounts of chlorine. The amount required to provide a chlorine residual of 1 part per million after thirty minutes' contact with this water was found to be approximately 2.5 parts per million. Accordingly, 2.5 parts per million of available chlorine (90 cc. of a chlorine solution prepared by dissolving grade A calcium hypochlorite in distilled water and standardized so as to contain 500 parts per million of available chlorine) were added to the 18,000 cc. of contaminated water. Thorough mixing was accomplished by rotation and agitation. The chlorine residual in this water after the thirty minute contact period was 1.08 parts per million.

The results of experiment A indicated the need for additional investigations. For this reason experiments B and C were carried out. The latter were started about four weeks after experiment A was completed.

EXPERIMENT B (*Effect of Superchlorination*).—To each of three bottles (water specimens 3, 4 and 5) containing 19,000 cc. of distilled water, 10.5 cc. of the same feces suspension[3] was added. Each water specimen thus contained approximately 55 parts of feces per million parts of distilled water. Two cc. of a suspension of Escherichia coli in isotonic solution of sodium chloride also was added to the contents of each bottle so that this organism could be used as an index of the effect on bacteria of the subsequent treatment of the specimens. The contaminated specimens were mixed thoroughly by rotation and agitation and then were allowed to stand for twenty-four hours at room temperature. Portions removed from each specimen then were pooled. Portions of this untreated pooled specimen were used for chemical and bacteriologic tests, for coagulation studies (unstrained portion) and for preliminary chlorine demand tests (strained portion). The subsequent treatment of the three specimens was as follows:

1. Water Specimen 3. Twenty-four hours after preparation, the specimen again was mixed thoroughly and then was strained through several layers of gauze and cotton. This constituted the only treatment of the specimen. The final strained water was opalescent and had a faint brown color and a strong hydrogen sulfide odor. Chemical studies showed that the straining process had resulted in a 32 per cent decrease in the concentration of organic solids and a slight decrease in turbidity.

2. Water Specimen 5: Twenty-four hours after its preparation, this specimen was strained through several layers of gauze and cotton. Chlorine demand and chlorine residual experiments on an untreated strained portion of the pooled specimen indicated that a concentration of approximately 25 parts per million of chlorine in the specimen would be required to oxidize completely all of the substances having a demand for chlorine, as shown by the "breakpoint" on a chlorine dosage-chlorine residual curve. Accordingly, sufficient chlorine (930 cc. of freshly prepared calcium hypochlorite solution standardized to contain 500 parts per million of available chlorine) to provide the 18.6 liter specimen with 25 parts per million of available chlorine was added and thoroughly mixed

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1. MacCallum, F. O., and Bradley, W. H.: Transmission of Infective Hepatitis to Human Volunteers, Lancet **2**: 228, 1944. Havens, W. P., Jr.; Ward, R.; Drill, V. A., and Paul, J. R.: Experimental Production of Hepatitis by Feeding Icterogenic Materials, Proc. Soc. Exper. Biol. & Med. **57**: 206 (Nov.) 1944. Neefe, J. R.; Stokes, J., Jr., and Reinhold, J. G.: Oral Administration to Volunteers of Feces from Patients with Homologous Serum Hepatitis and Infectious (Epidemic) Hepatitis, Am. J. M. Sc., to be published.

2. Neefe, J. R., and Stokes, J., Jr.: An Epidemic of Infectious Hepatitis Apparently Due to a Water Borne Agent: Epidemiologic Observations and Transmission Experiments in Human Volunteers, this issue, p. 1063.

3. This preparation, feces pool 1 FIH, was stored at — 5 to — 20 C. between the experiments.

with the water. After a thirty minute contact period the chlorine residual was found to be 15.23 parts per million. This indicated that approximately 0.25 Gm. of available chlorine was contained in the remaining 16.6 liter specimen after withdrawal of samples for chemical tests and bacteriologic examination. Since this concentration of chlorine in drinking water would not be tolerated, the specimen was dechlorinated as promptly as possible, after the thirty minute contact period, by the addition of 0.44 Gm. of sodium sulfite. This quantity of sodium sulfite was based on the requirement of 1.78 parts by weight of sodium sulfite for the neutralization of 1 part of chlorine. The sodium sulfite immediately reduced the chlorine residual to less than 1 part per million, and this was accomplished within forty-five minutes after the chlorine had been added. Additional small quantities (not measured) of sodium sulfite were introduced until the residual chlorine was completely neutralized. Complete dechlorination of the specimen was accomplished within sixty minutes after the chlorine had been added, completing the treatment of this water. The final specimen was colorless but had about the same degree of opalescence as water specimen 3.

The concentration of total organic solids and the turbidity of this specimen were approximately the same as those of specimen 3, indicating that the changes, as compared with the untreated pooled specimen, were due chiefly to the straining procedure. The treatment did decolorize the specimen and lowered the p_H from 6.7 to 6.52.

EXPERIMENT C (*Effect of Coagulation and Adsorption*).—A commonly used method for removing extraneous materials from drinking water involves coagulation of the water by sodium carbonate and aluminum sulfate. For this reason water specimen 4, twenty-four hours after its preparation, was coagulated[4] by adding 166 cc. of a solution of sodium carbonate containing 1.712 Gm. per 500 cc. and 332 cc. of a solution of aluminum sulfate containing 1.712 Gm. per 500 cc. These amounts provided the 16.6 liter specimen with 2.0 and 4.0 grains (0.13 and 0.26 Gm.) per gallon respectively of sodium carbonate and aluminum sulfate. The sodium carbonate was added first, and after thorough mixing the aluminum sulfate was introduced. Because of the possibility that activated carbon might aid in the removal of the hepatitis agent, 0.415 Gm. (equivalent to 25 parts per million in 16.6 liters) of activated carbon (Nuchar C-115) was added immediately after the aluminum sulfate and before the latter was mixed thoroughly with the water. The specimen then was agitated gently by rolling the bottle for approximately fifteen minutes. This distributed the carbon particles evenly throughout the mixture. A heavy flocculum, to which the carbon particles became attached, gradually formed and began to settle. The specimen was permitted to stand without disturbance for one hour. By that time all of the flocculated material and carbon had settled to the bottom of the bottle. The supernatant then was removed by a sterile siphon apparatus and was strained through a sterile gauze and cotton "filter" into a sterile bottle. This completed the treatment of the specimen. The strained supernatant was clear, colorless and odorless.

The chemical studies on water specimen 4 showed that coagulation and adsorption by means of the sodium carbonate-aluminum sulfate-activated carbon treatment, followed by sedimentation and straining, had removed 85 per cent of the total organic solids and had eliminated the turbidity, leaving the water crystal clear in appearance. The treatment also lowered the p_H of the specimen from 6.7 to 6.44.

Bacteriologic Studies on Water Specimens 3, 4 and 5.—These consisted of presumptive and confirmatory tests for Escherichia coli and total 37 C. bacterial counts (twenty-four hours) conducted according to a standard technic.[5] Presumptive tests for Escherichia coli in the untreated pooled specimen and in specimens 3 and 4 were positive, 40, 25 and 30 per cent gas formation being observed after twenty-four hours in the lactose fermentation tubes inoculated with 0.1 cc. of the respective specimens. Positive evidence of the presence of Escherichia coli in this portion of the three specimens was shown on confirmed and completed tests. The bacteria were so numerous that it was not possible to count the number of colonies developing after twenty-four hours at 37 C. on plates inoculated with 1 cc. of the three specimens. This would suggest that the sodium carbonate-aluminum sulfate-activated carbon treatment had failed to decrease the concentration of Escherichia coli. However, 37 C. bacterial counts on dilutions of this specimen were not made and a considerable decrease in bacterial count could have occurred without being apparent in the test of the undiluted water.

No bacterial growth was obtained in lactose tubes or on plates inoculated with water specimen 5, indicating that the bacteria had been destroyed by the chlorination procedure.

No bacterial studies of water specimens 1 and 2 were made at the time they were prepared and consumed. However, in order to obtain information concerning the effect on bacteria of treatment similar to that of water specimen 2, a portion of the untreated pooled specimen was treated with 2.5 parts per million of chlorine. After thirty minutes' contact, the chlorine residual was found to be 0.74 part per million. The presumptive test on this specimen was positive, the lactose tube inoculated with 0.1 cc. showing 60 per cent gas formation after twenty-four hours. However, the confirmatory test for Escherichia coli was negative, and the 37 C. count showed only four colonies per cubic centimeter of the undiluted specimen. No colonies developed on the plate inoculated with 1 cc. of a 1 to 10 dilution of the specimen. This specimen differed from water specimen 2 in that the former was inoculated with 2 cc. of a suspension of Escherichia coli in addition to the feces suspension and then was allowed to stand for twenty-four hours. The difference in thirty minute chlorine residuals in this and water specimen 2, 0.74 part per million and 1.08 parts per million respectively, probably was due to the development of a greater chloride demand with standing. The findings that the treatment of this specimen with 2.5 parts per million of chlorine apparently destroyed the Escherichia coli organisms and greatly reduced the bacterial count indicate the probable effect of this treatment on the bacteria in water specimen 2.

METHODS

The only known method of determining the presence of the hepatitis agent in a given material is by demonstrating the ability of that material to produce hepatitis in human volunteers. Thus the effect on the hepatitis agent of the water treatment was estimated by comparing the incidence, incubation periods and severity of hepatitis following the ingestion of the treated water by volunteers with the same factors following the ingestion of untreated water by other volunteers (controls).

Volunteers.—The volunteers selected as subjects for these experiments were all under 33 years of age. They had no previous history of jaundice and no evidence of liver dysfunction detectable by history, physical examination and liver function tests.

4. The amounts of sodium carbonate and aluminum sulfate required for satisfactory coagulation of the water were determined by tests on the untreated pooled specimen.

5. American Public Health Association: Standard Methods of Water and Sewage Analysis.

Inoculation of Volunteers.—The various water specimens were administered to groups of volunteers as follows:

1. EXPERIMENT A.—Forty minutes after the chlorine solution had been added, 400 cc. of water specimen 2 was ingested by each of 5 healthy male volunteers (group II). At the same time 400 cc. of water specimen 1 (untreated) was ingested by each of 5 other healthy male volunteers (group I). During a period of thirty-six hours a total of 3,600 cc. of the appropriate water was ingested, under supervision, by each subject.

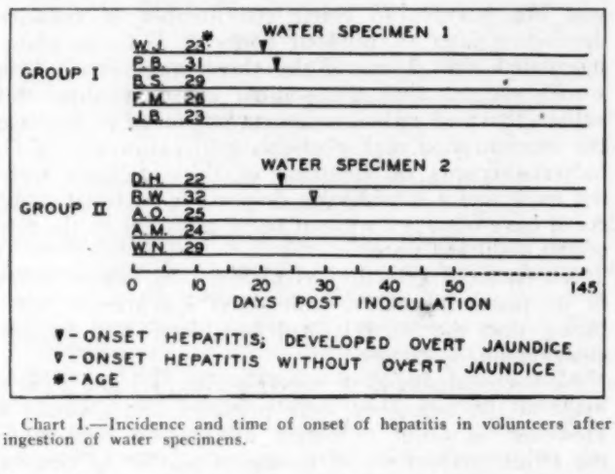

Chart 1.—Incidence and time of onset of hepatitis in volunteers after ingestion of water specimens.

2. EXPERIMENT B.—Twenty-eight hours after its preparation and four hours after it was strained, 400 cc. of water specimen 3 was ingested by each of 5 male volunteers (group III). Thirty-two hours after its preparation and fifteen minutes after it had been completely dechlorinated, 400 cc. of water specimen 5 was ingested by each of 5 male volunteers (group V). During a period of twenty-four hours, each of the volunteers in groups III and V ingested, under supervision, a total of 2,900 cc. and 2,800 cc. respectively of the appropriate water.

3. EXPERIMENT C.—Twenty-nine hours after its preparation and two hours after sedimentation following the addition of the sodium carbonate-aluminum sulfate-activated carbon mixture, 400 cc. of water specimen 4 (strained supernatant) was ingested by each of 5 male volunteers (group IV). During a period of twenty-four hours the men of group IV ingested a total of 2,725 cc. of water specimen 4. Group III served as the control group for both groups IV and V.

Isolation of Volunteers.—The various groups of volunteers were isolated from one another, and from other persons, during and after the period of inoculation; however, the members of each group were not isolated from one another. The groups were confined to separate quarters and had separate dining rooms, eating utensils and toilet facilities. No articles were exchanged between the groups.

Detection of Hepatitis.—Each subject was studied at frequent intervals by means of the group of liver function tests described elsewhere.[6] These studies had been conducted at frequent intervals during a three to six week preinoculation period in order to establish, as far as possible, the physiologic variation in the response of each person to each of these tests. After inoculation, all subjects were observed closely for symptoms and signs of any illness and the liver function tests were performed two or more times weekly. Temperatures were taken twice daily.

6. Neefe, J. R.; Stokes, J. Jr.; Reinhold, J. G., and Lukens, F. D. W.: Hepatitis Due to Injection of Homologous Blood Products in Human Volunteers, J. Clin. Investigation **23**: 836 (Sept.) 1944.

RESULTS

Effect of Chlorination (Experiment A).—As shown in chart 1, 2 of the 5 controls (group I) who ingested 3,600 cc. of water specimen 1 (untreated) developed infectious hepatitis[7] during the 4th week after inoculation. During the same period 2 of the 5 men (group II) who ingested 3,600 cc. of water specimen 2 (chlorinated) also developed infectious hepatitis. Three of the 4 men who contracted hepatitis had moderately severe jaundice. The 4th (R. W.), who had received chlorinated water, did not develop overt jaundice, but the occurrence of typical symptoms and elevation of temperature to 102 F., strongly positive tests for bilirubin in the urine, 43 per cent retention of sulfobromophthalein after forty-five minutes, a 4 plus cephalin flocculation reaction and a significant decrease in the concentration of esterified serum cholesterol confirmed the diagnosis of hepatitis in this case. Subject D. H. (chlorinated water) had slight elevations of temperature and mild symptoms of malaise, anorexia and abdominal discomfort periodically after the 8th postinoculation day. On the 23d day acute symptoms and signs of the infection suddenly developed. These included a chill, an oral temperature of 104 F., a scarlatiniform rash, abdominal pain, anorexia, nausea and vomiting. By the 27th day he was obviously jaundiced. It is of interest that the earliest, and subsequently the most severe, manifestations occurred in this volunteer who had received the chlorinated water.

Effect of Superchlorination (Experiment B).—Four of the 5 controls (group III) who ingested 2,900 cc. of water specimen 3 (untreated except for straining) developed moderately severe infectious hepatitis after incubation periods of 19, 19, 19 and 22 days (chart 2). All of these 4 men developed overt jaundice. The highest total bilirubin concentration in each was 6.3, 7.2, 9.3 and 10.2 mg. per hundred cubic centimeters of serum. All had moderate to pronounced liver tenderness during the active disease. The 5th man in this group has shown no clinical or laboratory manifestations of hepatitis during the 80 days which have elapsed since ingestion of the water.

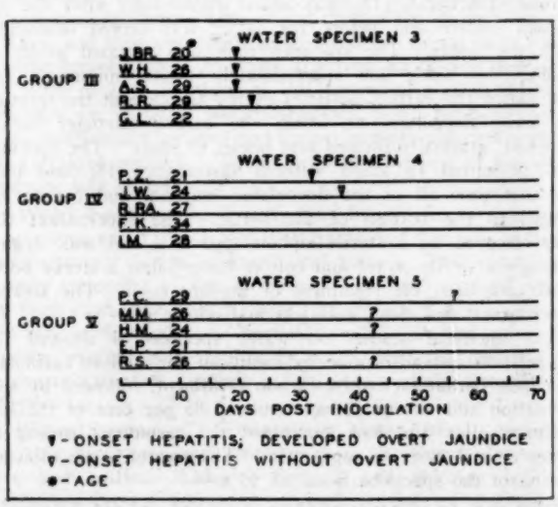

Chart 2.—Incidence and time of onset of hepatitis in volunteers after ingestion of water specimens.

7. The diagnosis of infectious hepatitis was based on the occurrence of typical symptoms and signs of the disease in association with typical changes in the responses to the various liver function tests.

None of the 5 men (group V) who ingested 2,800 cc. of water specimen 5 (superchlorinated, then dechlorinated) have had symptoms or physical signs of any illness during the 80 days which have elapsed.

However, serums obtained from subject H. M. on the 42d, 49th, 52d, 53d, 57th, 64th and 67th days gave cephalin cholesterol flocculation reactions of 2+/3+,[8] 1+/2+, ±/2+, 2+/2+, ±/2+, 2+/3+ and 2+/3+ respectively. Six tests performed on different days during a three week preinoculation period gave readings of 0/±, 0/0, 0/1+, 0/0, 0/0 and 0/0 respectively. During the postinoculation period all the other liver function tests performed in association with the cephalin tests gave normal results.

Serums obtained from subject M. M. on the 42d, 49th, 59th and 67th days gave cephalin cholesterol flocculation readings of 0/1+, 0/1+, ±/3+ and 1+/2+ respectively. Twenty tests performed on different days prior to the 42d day had given negative readings at both twenty-four and forty-eight hours. On the 56th day the serum esterified cholesterol constituted 39 per cent of the total cholesterol. With several previous determinations the esterified fraction had constituted 57 to 68 per cent of the total cholesterol. The other tests of liver function have shown no abnormalities during the eighty days which have elapsed.

Serums obtained from subject R. S. on the 42d, 59th and 67th days gave cephalin flocculation readings of 0/1+, 0/1+ and 1+/2+ respectively. Many previous cephalin tests had shown no flocculation. The other tests of liver function showed no abnormalities during the postinoculation period.

Serum obtained from subject P. C. on the 56th day gave a cephalin cholesterol flocculation reading of 2+ at forty-eight hours. All previous and subsequent cephalin tests were negative. The other tests of liver function revealed no abnormalities during the postinoculation period.

Subject E. P. has shown no clinical or laboratory manifestations of any illness during the eighty days which have elapsed to date.

Effect of Coagulation-Adsorption (Experiment C).—Two of the 5 men (group IV) who received 2,725 cc. of water specimen 4 (treated with sodium carbonate, aluminum sulfate and activated carbon) developed mild infectious hepatitis after incubation periods of thirty-three and thirty-seven days (chart 2).

Mild symptoms and fever appeared in subject P. Z. on the 33d day, but the diagnosis of hepatitis could not be established until the 41st day, when bilirubinuria, sulfobromophthalein retention and cephalin cholesterol flocculation simultaneously appeared. Although his total serum bilirubin concentration never exceeded 1.9 mg. per cubic centimeter, the other tests of hepatic function revealed the presence of considerable hepatic disturbance as indicated by (*a*) bilirubinuria 4+, (*b*) sulfobromophthalein retention 42 per cent at forty-five minutes, (*c*) cephalin cholesterol flocculation 4+, (*d*) serum colloidol gold reaction 4+, (*e*) thymol turbidity test 10 units, (*f*) serum esterified cholesterol 36 mg. per hundred cubic centimeters (15 per cent of total). Faint scleral icterus was observed for a few days, but no tenderness or enlargement of the liver was detected at any time. The only significant gastrointestinal symptom was anorexia. Nausea and vomiting did not occur. The most prominent symptoms were malaise and headache associated with mild pain in the eyeballs on movement. At the onset, his temperature reached 103 F. (oral), but it returned to normal within thirty-six hours and remained normal thereafter.

The symptoms and signs in subject J. W. were even less pronounced that those of P. Z. On the 37th day he developed slight malaise, anorexia, vague abdominal discomfort, slight headache, mild diarrhea and an elevation of temperature to 100 F. (oral). The headache, fever and diarrhea persisted only twenty-four hours, but the malaise, anorexia and vague abdominal discomfort lasted for approximately ten days. No abnormal physical findings were detected at any time. During the illness, the cephalin cholesterol flocculation test gave responses varying from 1 to 3+ (previously always negative), the thymol turbidity test gave a reading of 3 units (highest previous reading was 1.5 units) and the concentration of esterified serum cholesterol decreased to 29 per cent of the total cholesterol (previously 53 to 63 per cent of the total). The other tests of liver function showed no significant abnormalities.

No significant clinical or laboratory abnormalities have been observed in the other 3 men of this group during the eighty days which have elapsed.

8. 2+/3+ signifies the twenty-four and forty-eight hour readings respectively.

COMMENT

In experiment A no significant differences in incidence, incubation period or severity of the disease were observed between the groups receiving the untreated and the chlorinated water. The results indicate, therefore, that this causative agent of infectious hepatitis was not inactivated or attenuated by a forty minute period of contact with sufficient chlorine to provide a residual chlorine concentration of 1 part per million after thirty minutes' contact. Thus this technic for emergency disinfection of drinking water does not assure protection against the agent of infectious hepatitis.

The results in group V (experiment B) indicate that superchlorination resulted in a definite attenuation of the hepatitis agent. None of the men ingesting the superchlorinated water have had symptoms or physical signs of any illness. However, between the 42d and 67th days after inoculation, positive cephalin cholesterol flocculation tests were obtained with serums from 4 of the 5 men. The significance of the positive tests under these conditions is most uncertain. Positive tests were not obtained with normal serums tested simultaneously, and no change was made in the technic of performing the test during this period. Thus the possibility that the positive tests in these men were due to subclinical hepatic disturbances, produced by an attenuated hepatitis agent, cannot be excluded. For this reason the results of this experiment do not permit the conclusion that the hepatitis agent was inactivated completely by superchlorination. However, the results do warrant the conclusion that the hepatitis agent, at the least, was much attenuated by superchlorination.

The results in group IV (experiment C) indicate that the hepatitis agent was not completely removed or inactivated by treatment of the contaminated water with sodium carbonate, aluminum sulfate and activated carbon. However, the incidence of hepatitis was lower, the incubation periods were longer and the disease was much less severe than in the control group (group III). Although the groups were too small for these differences to be conclusive, the differences were consistent. The results suggest, therefore, that the treatment procedure may have resulted in either or both a decrease in concentration and a decrease in virulence of the hepatitis agent. Previous studies [2] have afforded some evidence that a decrease in the amount of orally administered hepatitis agent does not necessarily influence the severity of the disease but may result in a prolonga-

tion of the incubation period. Thus the mildness of the disease in the men of group IV may have been due to an attenuating effect of this treatment procedure on the hepatitis agent.

The results of these studies suggest that the control of the hepatitis agent in contaminated water may require modification of certain methods commonly used for water disinfection. They also suggest that the methods used may affect the concentration and the virulence of the hepatitis agent. These effects may result in modification of the incubation period and the severity of the disease. The possible prolongation of the incubation period should be borne in mind in the interpretation of epidemiologic data. It also is possible that the ratio of icteric to nonicteric cases in epidemics due to water borne agents may be influenced by the treatment to which the water has been subjected.

SUMMARY

Three experiments (A, B and C) were conducted on the disinfection of water containing the causative agent of infectious hepatitis. In experiment A, 2 equal volumes of distilled water were contaminated with feces known to contain the causative agent of infectious (epidemic) hepatitis. One specimen (water specimen 2) was treated with sufficient chlorine to provide a chlorine residual of 1 part per million after thirty minutes' contact. The other specimen (water specimen 1) was not subjected to further treatment. Two of the 5 volunteers (control group) who ingested 3,600 cc. of the untreated water developed infectious hepatitis after incubation periods of twenty-one and twenty-three days. Two of the 5 volunteers who ingested 3,600 cc. of the chlorinated water developed infectious hepatitis, 1 with and 1 without overt jaundice, after incubation periods of twenty-three and twenty-eight days respectively.

The results of experiment A led to experiments B and C. Three equal volumes of distilled water were contaminated with feces containing the hepatitis agent as in experiment A. The only treatment of 1 specimen (water specimen 3) consisted in straining it through a gauze and cotton "filter." Another specimen (water specimen 5) after similar straining was treated with sufficient chlorine to reach the chlorine "breakpoint" and provide a chlorine residual of 15 parts per million after thirty minutes' contact (superchlorination). The remaining specimen (water specimen 4) was treated with sodium carbonate, aluminum sulfate and activated carbon; after settling, the supernatant was strained through gauze and cotton. Four of the 5 volunteers (control group) who ingested 2,900 cc. of water specimen 3 (untreated except for straining) developed moderately severe infectious hepatitis with overt jaundice after incubation periods of nineteen, nineteen, nineteen and twenty-two days. None of the 5 men ingesting 2,800 cc. of water specimen 5 (superchlorinated) have developed clinical symptoms or physical signs of hepatitis during the eighty days which have elapsed. However, 4 of the 5 men developed positive cephalin cholesterol flocculation tests between the 42d and 67th days after their inoculation. One of these 4 also showed a decrease in the concentration of esterified serum cholesterol. Other liver function tests revealed no other evidences of hepatic dysfunction at any time. Two of the 5 men who ingested 2,725 cc. of water specimen 4 developed mild infectious hepatitis, 1 with scleral jaundice and 1 without overt jaundice, after incubation periods of thirty-three and thirty-seven days respectively.

CONCLUSIONS

1. Treatment of contaminated water with sufficient chlorine to provide a chlorine residual of 1 part per million after thirty minutes' contact did not inactivate or attenuate the causative agent of infectious hepatitis.

2. Treatment of contaminated water with sufficient chlorine to provide a residual chlorine concentration of 15 parts per million after a thirty minute contact period resulted in a definite attenuation of the hepatitis agent.

3. Treatment of contaminated water with sodium carbonate, aluminum sulfate and activated carbon did not completely remove or inactivate the hepatitis agent. However, the treatment may have resulted in a decrease in concentration and possibly some decrease in virulence of this agent.

4. The concentration and/or virulence of the hepatitis agent in water may be so affected by these treatment procedures as to result in some modification of the disease produced. The available evidence suggests that a decrease in either or both concentration and virulence may be associated with a prolongation of the incubation period. A decrease in virulence also may be associated with a decrease in the severity of the disease.

5. The complete inactivation of the causative agent of infectious hepatitis in drinking water may require further modifications of methods used for water disinfection.

TOXIC EFFECTS OF DIODOQUIN

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ALAN LESLIE, M.D.
NEW ORLEANS

According to previously published reports of cases of amebic dysentery treated with diodoquin, the use of this drug has not been accompanied by any toxic or disagreeable symptoms. Craig,[1] in recommending the use of diodoquin for the prophylaxis of amebiasis, stated that ". . . diodoquin is not accompanied by any disagreeable symptoms, even when administered in large doses over a longer period of time." Silverman[2] reported 25 cases of acute and chronic amebic colitis and observed no toxic effects after a high dosage of twelve tablets a day. Hummel[3] treated 20 patients with nine tablets a day for twenty days without observing any evidence of toxicity. D'Antoni[4] made no mention of drug reaction in 84 cases of amebiasis treated with diodoquin. Bercovitz[5] in his recent textbook, referring to diodoquin, states that "the drug is nontoxic and nonirritating to the bowel mucosa." In view of such statements made by competent workers the following manufacturer's advertisement claim does not seem extravagant. In the G. D. Searle & Co. advertisement

From the Gastro-Intestinal Department, Touro Infirmary.

1. Craig, C. F.: The Medicinal Prophylaxis of Amebiasis, Am. J. Trop. Med. **20**: 799 (Nov.) 1940.

2. Silverman, D. N.: The Treatment of Amebic Colitis with Diiodohydroxyquinoline (Diodoquin), Am. J. Digest. Dis. **4**: 281 (July) 1937.

3. Hummel, H. G.: A Critical Appraisal of the Newer Amebicides and the Results of Treatment of Amebiasis with Di-Iodo-Hydroxyquinoline (Diodoquin), Am. J. Digest. Dis. **6**: 27 (March) 1939.

4. D'Antoni, J. S.: Further Observations on Amebic and Bacillary Colitis in the New Orleans Area, Am. J. Trop. Med. **23**: 237 (March) 1943.

5. Bercovitz, Z. T.: Clinical Tropical Medicine, New York, Paul B. Hoeber, Inc., 1944, p. 25.

appearing on page 9 of the advertisement section of the June 17, 1944 issue of THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION this statement is made: "Whenever amebiasis is suspected, the high iodine amebicide . . . DIODOQUIN (5, 7-diiodo-8-hydroxyquinoline) . . . can be used without fear of untoward effects—its toxicity is negligible. . . . May be given in large doses over prolonged periods." In order to correct any misapprehension as to the absence of toxicity of this drug, without attempting to controvert its therapeutic efficacy, we believe that it is important to present 3 cases of toxic reactions following the administration of diodoquin, especially since these hitherto incontestable claims of freedom from toxicity have been made in THE JOURNAL, a medium widely circulated to the medical profession.

REPORT OF CASES

CASE 1.—P. F., a white man aged 52, admitted to the hospital with a six month history of bowel disturbance and with motile amebas in the stool, was given simultaneous emetine hydrochloride and diodoquin therapy, the former drug being administered intramuscularly in a dose of 30 mg. (½ grain) daily for five days only. Diodoquin was administered for nineteen days in a dosage of four tablets of 0.2 Gm. (3.2 grains) each three times a day. Shortly after chemotherapy was commenced the patient became asymptomatic. Eight days after discontinuation of the diodoquin, examination of the saline purged stool failed to reveal the presence of amebas. Twelve days later a furuncle appeared over the left temporal region. This furuncle ruptured spontaneously. Two months after the drug was stopped the patient returned with a recent history of two episodes of chills and fever and right upper quadrant distress. With a presumptive diagnosis of amebic hepatitis, and pending admission to the hospital, diodoquin was again prescribed in the same dosage as previously. Three days later a furuncle appeared over the left anterior superior iliac spine. This was incised and drained. The diodoquin was immediately discontinued, but two more furuncles, which ruptured spontaneously, made their appearance. Carbarsone was substituted for the diodoquin, and the emetine hydrochloride, which was started on admission to the hospital, was continued. Diarrhea which appeared was attributed to the carbarsone. This drug was discontinued, and the diarrhea subsided. At the time of discharge from the hospital the patient was asymptomatic. No amebas were seen in the saline purged stool, but it was thought that too little time had elapsed since the discontinuation of chemotherapy to warrant a definite statement as to the status of the patient.

CASE 2.—O. B. C., a white man aged 42, a pipefitter, had a history of "bowel trouble" of twenty years' duration. Stool examination revealed the presence of trophozoites of Ameba histolytica. Emetine hydrochloride and diodoquin therapy, as outlined in the first case, was instituted. The former was administered daily for four days. After eight days of diodoquin therapy the patient developed a severe generalized furunculosis necessitating multiple incisions and drainage. Although the drug was discontinued at once, the furunculosis persisted for a considerable time. Examination of the saline purged stool six months after therapy was discontinued failed to reveal the presence of amebas. The patient became asymptomatic, so despite the toxicoderma and short therapeutic course it is believed that a cure was obtained.

CASE 3.—M. R., a white woman aged 51, Spanish born, with amebic infection of the bowel, proved by feces examination, received twelve tablets of diodoquin daily for twenty-three days. The day after discontinuation of the drug the patient complained of sore throat and chilly sensations. A fine skin rash appeared; this rapidly developed into a blotchy erythema involving the entire body. The patient was readmitted to the hospital one week after completing the course of diodoquin. The temperature, which ranged up to 101.6 F. (oral), subsided after seven days of expectant treatment. Laboratory studies including blood culture showed no significant abnormality. The process subsided and the patient was discharged ten days after admission. One year later she was well and free from amebas.

COMMENT

In the first case no furuncles were observed except in association with diodoquin therapy, so it is reasonable to infer that a cause and effect relationship existed. Although the action of diodoquin is in the main topical, it is apparent that at least in certain inidviduals a sufficient degree of absorption takes place to result in what purported to be an iodine toxicoderma. This patient demonstrated a hypersensitivity not only to the iodine contained in diodoquin but to the arsenic contained in carbarsone and typifies the sort of drug sensitive individual not infrequently encountered. In the second case the role of diodoquin in the etiology of the furunculosis was so obvious as to leave little room for question. Of interest in this case was the apparently high iodine absorption and retention with delayed excretion from a preparation which is generally considered to be absorbed slightly or not at all. The type of reaction in the third case differed from those in the first two presented in that there was a systemic as well as a cutaneous toxicity exhibited and that the skin reaction was erythematous rather than pustular. We believe, however, that in this as well as the other cases idiosyncrasy to the iodine contained in the drug was the basis for the toxic manifestations.

The reason for the difference between the experience of other observers, as well as the early experience of one of us (D. N. S.), and the recent observations reported herein is not entirely clear. The dose originally recommended was one or two tablets of diodoquin three times daily. It was observed by Silverman that a larger dosage of the drug was required for maximum results. A dosage of three or four tablets three times a day was found to be effective in the eradication of amebas when the smaller dosage was not; this with no apparent introduction of toxic effects on the host. The element of statistical chance may account for the difference in question, for although the 3 cases were observed within a period of less than a year the overall incidence of toxic reactions is low. This report does not in any way attempt to negate the claims for the therapeutic efficacy of the drug in the treatment of amebiasis, since we as well as many others have used the drug with considerable success. It is, however, the desire to call attention to the possibility of symptoms of drug poisoning appearing during the treatment of amebiasis with diodoquin.

1521 Delachaise Street.

Development and Use of Cocaine.—The development and use of cocaine as a local anesthetic agent was chiefly the work of Carl Koller. When Koller was house surgeon at the Vienna General Hospital, his friend Sigmund Freud was studying the possibility of curing patients addicted to morphine by treating them with cocaine. Both Koller and Freud studied the physiologic aspects of cocaine. Freud turned his attention away from these investigations. Koller, however, continued his studies. He injected a weak solution of cocaine into the eye of a frog and noticed that the eye became insensitive to pain. On Sept. 15, 1884 Koller reported his observations to the Ophthalmological Congress held in Heidelberg. Soon afterward cocainization of the eye for the production of local anesthesia was generally adopted.—Keys, Thomas E.: The History of Surgical Anesthesia, New York, Schuman's, 1945.

LOEFFLER'S SYNDROME ASSOCIATED WITH CREEPING ERUPTION (CUTANEOUS HELMINTHIASIS)

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AND
MAJOR EDWIN M. GOLD
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We have had the opportunity of observing 9 cases of creeping eruption in the dermatology wards and clinics of the Army Service Forces Regional Hospital, Camp Blanding, Florida, that have developed transient pulmonary infiltration during the course of their infection. A preliminary report of these observations is indicated since (*a*) standard textbooks [1] lead one to believe that this nematodal infection (usually Ancylostome braziliense) is a localized intradermal invasion; (*b*) a review of the available literature does not reveal a report of associated pulmonary involvement; (*c*) the clinical course, laboratory and x-ray findings are similar to the migratory pulmonary infiltrations with eosinophilia reported by Loeffler and others.[2]

The dermatologic manifestation of creeping eruption is an accepted clinical entity adequately described in standard textbooks. Kirby-Smith [3] suggested the nematodal origin of these lesions. The larvae wandering through the layers of the skin produce the serpiginous, elevated reddish tunnels that are characteristic of the disease. Dove and White [4] proved that the filariform larvae of Ancylostoma braziliense produce these lesions. The dog and cat are natural hosts for these nematodes and inoculate the soil with their feces. The filariform larvae remain viable for long periods in soil that is moist, sandy and shady, awaiting an opportunity for contact with the human skin.

During the past twelve months 26 cases of creeping eruption with classic cutaneous manifestations have been seen. Fifteen of these cases were observed for a period of fourteen days or more. Nine of these 15 cases during their period of observation demonstrated transient migratory, pulmonary infiltration, peripheral eosinophilia and paucity of clinical signs or symptoms of systemic disease, fulfilling the criteria of Loeffler's syndrome. In this series chest roentgenograms were made every three days for at least fourteen days. Our experience corroborates Loeffler's original observation that serial x-rays are necessary to detect the transient migratory pulmonary infiltration.

These 9 cases were afebrile during the entire period of observation. Physical findings were minimal. Slightly decreased resonance, roughened breath sounds and insignificant increase in the respiratory rate were the only positive findings. Rales were not heard at any time. Except for local skin irritation and a mild cough that occurred in only 4, these patients were not aware of any illness.

Differential counts on peripheral blood smears revealed an eosinophilia varying from 1 per cent to 32 per cent. The degree of eosinophilia roughly approximated the extent of the skin and pulmonary lesions and tended to persist after these lesions had subsided.

Roentgen examination of the chest revealed a patchy infiltration, transient and often migratory in nature, usually not appearing before the seventh day of the skin invasion. When erroneous diagnosis or procrastination in therapy of the local skin lesions occurred, the pulmonary infiltration continued a migratory course over a period of weeks.

Vital capacity studies performed in 5 cases on several occasions failed to reveal any diminution, though chest x-rays were positive at the time. This fact, together with lack of dyspnea and/or cyanosis, tends to support the contention that the infiltrative process is an interstitial one rather than a true alveolar exudative or atelectatic consolidation.

Sedimentation rates by the Wintrobe method repeated every three days on 5 of the 9 patients with pulmonary infiltration were within normal limits except in 2 cases complicated by secondary infection and cellulitis about the cutaneous lesions. The rate in these 2 cases returned to normal as soon as the secondary infection

TABLE 1.—*Observations in Case 1*

Day of Disease	Date	Blood Eosinophilia, %	Sputum Eosinophilia, %	X-Ray of Chest. Site of Infiltration	60 Minute Sedimentation Rate, Mm.
1	8/ 2/43	6	..	.....	..
8	8/ 9/43	..	..	Patchy, bilateral, central hilar	..
11	8/11/43	15	..	.....	20
13	8/13/43	..	..	Patchy, bilateral, decrease.....	..
15	8/15/43	23	— 0	Negative.....	..
17	8/17/43	..	..	.....	40
20	8/20/43	2	..	.....	..
21	8/21/43	..	35	.....	..
23	8/23/43	26	..	Patchy, bilateral, minimal.....	29
24	8/24/43	..	75	.....	..
25	8/25/43	..	90	.....	..
26	8/26/43	..	90	Patchy, bilateral, minimal.....	38
28	8/28/43	..	90	.....	..
30	8/30/43	19	80	.....	..
31	8/31/43	..	80	Residual infiltration remains patchy, bilateral	31
32	9/ 1/43	..*	90	.....	..
34	9/ 3/43	..	..	.....	24
35	9/ 4/43	20	70	.....	..
37	9/ 6/43	21	70	Negative.....	8
41	9/10/43	13	65	.....	20
44	9/13/43	13	90	Negative.....	21
47	9/16/43	6	..	.....	4
51	9/20/43	10	..	.....	8
54	9/24/43	8	..	.....	11
57	9/27/43	7	..	.....	4
60	9/30/43	..	..	.....	12
64	10/ 4/43	1	..	.....	1
68	10/ 8/43	7	..	.....	6

Patient admitted Aug. 2, 1943 with diagnosis of trichophytosis pedis, secondary cellulitis, bilateral, severe. On eighth hospital day the diagnosis of creeping eruption was made.

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subsided despite persistence of the pulmonary infiltration.

By persistent effort 8 patients produced 39 sputum specimens at some time during their illness. Eosinophil counts on these specimens varied from 2 per cent to 90 per cent.

TABLE 2.—*Observations in Case 2*

Day of Disease	Date	Blood Eosinophilia, %	Sputum Eosinophilia, %	X-Ray of Chest. Site of Infiltration	60 Minute Sedimentation Rate, Mm.
14	6/28/44	— 0	..	L. L. L., R. U. L.....	10
18	8/ 2/44	3	— 0	L. L. L. (—), R. U. L...	1
21	7/ 5/44	1	10	L. L. L.....	6
24	7/ 8/44	18	20	L. L. L. reduction.....	15
27	7/11/44	19	..	L. L. L. reduction.....	14
30	7/14/44	26	..	L. L. L. reduction.....	13
33	7/17/44	16	35	L. L. L., R. U. L.....	5
36	7/20/44	30	25	R. U. L., R. L. L.....	10
39	7/23/44	32	20	R. M. L.....	9
42	7/26/44	30	25	R. M. L. reduction.....	..
45	7/29/44	38	10	R. M. L. residual.....	6
50	8/ 3/44	31	80	Negative.....	9
53	8/ 6/44	23	..	Negative.....	4

Patient admitted with painful, itchy, weeping, secondarily infected serpiginous dermatitis typical of creeping eruption over buttocks. Lesions present fourteen days prior to admission. Mild cough developed day after admission.

Examination of 81 stool specimens from the 26 patients encompassing periods of observation from ten days to three months failed to reveal presence of ova or parasites in any specimen. This corroborates the findings of Smith, Dove and White and others that intestinal infestation by this nematode in the human being is rare.

Brunner[5] found in immunologic studies of human parasitic infections that Ascaris extract is representative of the nematode group. He also proved that intradermal testing with extracts of nematodal parasites had a practical value as a diagnostic aid in that positive reactions were indicative of past or present infestation. Because of these findings, Ascaris and Trichina extracts standardized for nitrogen content were used for intradermal testing in all cases. Positive results were obtained with at least one of these extracts in 23 of the 26 cases varying from 1 to 4 plus. No correlation between degree of skin test sensitivity and clinical findings was observed. Similarly no specificity as to reaction with Ascaris or Trichina extracts was noted.

TABLE 3.—*Observations in Case 3*

Day of Disease	Date	Blood Eosinophilia, %	Sputum Eosinophilia, %	X-Ray of Chest. Site of Infiltration	60 Minute Sedimentation Rate, Mm.
21	6/22/44	13	..	Negative.....	..
26	6/27/44	..	..	Negative.....	..
28	6/29/44	..	..	Negative.....	..
32	7/ 3/44	..	..	R. U. L.....	..
36	7/ 7/44	9	..	Negative.....	..
39	7/10/44	16	..	R. M. L., R. L. L.....	..
42	7/13/44	12	..	Negative.....	..
45	7/16/44	20	..	R. L. L.....	..
49	7/20/44	9	..	R. L. L.....	9
52	7/23/44	23	..	Negative.....	7

Patient admitted on twenty-first day of disease with creeping eruption burrows over glutei, bilateral and on anterior abdominal wall. No cough. No sputum.

The migratory character of the pulmonary infiltration and the eosinophil variation in blood and sputum are summarized in 4 typical cases in tables 1 through 4.

COMMENT

The cases herein reported fulfil the criteria of Loeffler's syndrome predicated on the triad of a transient and migratory pulmonary infiltration, paucity of symptoms and physical signs and peripheral eosinophilia.

Similar findings have been reported associated with tuberculosis,[6] Ascaris infection,[7] Trichinosis,[8] asthma,[9] Malta fever,[10] Endameba histolytica infection[11] and pollinosis.[12] Such a diversified list of etiologic factors lends credence to the view that Loeffler's syndrome is an allergic phenomenon.

Additional proof of an allergic basis for Loeffler's syndrome and helpful points in its differential diagnosis from inflammatory lesions of the lung are peripheral and sputal eosinophilia, normal sedimentation rate, normal leukocyte count, absence of fever and systemic manifestations, migrating pulmonary infiltration, normal vital capacity and positive skin reactions to nematode antigens in cases associated with helminthiasis.

TABLE 4.—*Observations in Case 3*

Day of Disease	Date	Blood Eosinophilia, %	Sputum Eosinophilia, %	X-Ray of Chest. Site of Infiltration	60 Minute Sedimentation Rate, Mm.
7	6/27/44	2	..	R. L. L., L. L. L.....	..
10	6/30/44	7	..	R. L. L., L. L. L.....	..
13	7/ 3/44	..	..	R. L. L., L. L. L.....	..
16	7/ 6/44	..	..	R. L. L. (—), L. L. L. (—)..	..
18	7/ 8/44	..	..	Negative.....	..
22	7/12/44	..	..	Hilar, R and L.....	..
25	7/15/44	13	..	Hilar, R and L (—).....	..
27	7/17/44	..	..	Negative.....	..
30	7/20/44	..	10	.....	..
34	7/24/44	..	..	Negative.....	..

Clinic patient, first seen on seventh day of disease. Chief complaints pruritus and secondary infection of serpiginous burrows on dorsal surfaces both hands. No cough. No appreciable sputum.

SUMMARY

1. Nine cases of cutaneous helminthiasis have been observed with clinical findings fulfilling the criteria of Loeffler's syndrome.

2. These cases present a hitherto unreported etiologic factor in the production of Loeffler's syndrome.

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MENTAL AND PERSONALITY DISORDERS IN SELECTIVE SERVICE REGISTRANTS

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The diagnosis of mental and personality disorders or serious potentialities for their development has resulted in the rejection of more Selective Service registrants than has any other defect. It must be understood that by mental and personality disorders is meant any variation in the emotional capacity of the individual to adjust to his situation which results in symptoms indicating, in this instance, the possibility of maladjustment to military life.[1] Among white registrants no other defects approach mental and personality disorders in importance as a cause for rejection, while for Negroes they are exceeded only by mental deficiency and syphilis. In addition, mental and personality disorders have accounted for more disability discharges from the armed forces than any other defects.

TABLE 1.—*Estimated Number of Registrants Aged 18-37 in Rejected Classes Because of Mental and Personality Disorders, Jan. 1, 1945* *

Race	Total Rejected	Rejected for Mental and Personality Disorders	
		Number	Per Cent of Total
All races	4,493,000	801,700	17.8
White †	3,621,000	708,000	19.6
Negro	872,000	93,700	10.7

* Includes those in class IV-F and also those transferred from class IV-F to the occupationally deferred classes, II-A(F), II-B(F) and II-C(F).
† Includes all races other than Negro.

The standards for the rejection or acceptance of men for military service have been the responsibility of the armed forces. Most of the rejections for mental and personality disorders have been made by psychiatrists at the armed forces' induction stations. However, the more serious cases such as those which have necessitated institutionalization have nearly always been rejected by Selective Service local board physicians; and during peacetime many of those with less serious mental and personality disorders were also rejected at local boards in accordance with the armed forces' physical standards.

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This report is based on sample studies of the results of examination recorded on DSS Forms 200, Reports of Physical Examination, for Selective Service registrants physically examined at local boards in peacetime, and DSS Forms 221, Reports of Physical Examination and Induction, for registrants examined at local boards and induction stations during wartime. Coverage of the sample studies varies from 10 to 25 per cent of the examinations.

1. Mental and educational deficiency are not included in this report. The major subdivisions of mental and personality disorders as used in this report were determined to a large extent by Medical Circular No. 1 revised by the Selective Service System May 19, 1941, which divided mental and personality disorders into five categories. They are (1) grave mental and personality disorders, such as schizophrenia (dementia precox), paranoia and their various manifestations, (2) major abnormalities of mood, such as abnormal fluctuations in mood and constant states of depression and elation, (3) psychopathic personality, including constitutional psychopathic inferiority characterized by the record of certain types of recurrent social, sexual or legal difficulties, (4) psychoneurosis, including hysteria, morbid anxiety, hypochondriasis and the so-called psychosomatic disorders such as gastrointestinal and cardiovascular disorders due primarily to mental and personality difficulties and (5) alcoholism and drug addiction, including psychoses due to these states.

NUMBER CURRENTLY REJECTED

On Jan. 1, 1945 an estimated 801,700, or 17.8 per cent of the 4,493,000 registrants aged 18-37 in the rejected classes, were so classified because of mental and personality disorders (table 1). This figure does not include the thousands of registrants rejected for such disorders at one time or another but who were later reexamined and either inducted into the armed forces or rejected for some reason other than mental and personality disorders. These defects accounted for a greater proportion of white registrants rejected than of Negroes.

More than 8 out of every 10 rejections for mental and personality disorders were due to psychoneurotic disorders or psychopathic personality. While most of the registrants rejected for these defects are not sufficiently incapacitated to prevent their following a useful vocation in civilian life, it was determined by Army and Navy medical examiners that military life would probably aggravate their condition. The remaining registrants who were rejected for mental and personality disorders had the more serious disorders or history of such conditions. It is estimated that approximately 30,000 of these had been rejected by local board physicians because of an obviously disqualifying mental or personality disorder. The basis for this disqualification was authentic information that the registrant had been under treatment or in an institution at one time or another.

REJECTION RATES FOR MENTAL AND PERSONALITY DISORDERS

Rejection rates for mental and personality disorders have increased with each successive year of Selective Service operations.[2] During 1940 and 1941 approximately 22 of every thousand registrants examined were rejected for this defect (table 2). In 1942 the rate increased to 50, in 1943 to 74 and in 1944 to 120 per thousand examined.

From November 1940 on, no appreciable changes have been made in the armed forces' actual standards for acceptance of men with mental and personality disorders as prescribed in Mobilization Regulations 1-9. However, with the gradual increase of psychiatrists on the staffs of armed forces' examining stations during wartime there was a stricter interpretation and application of the standards, which resulted in increased rejections for mental and personality disorders. In addition, three factors have operated to increase the rejection rate for mental and personality disorders. They are (1) changes in physical examination procedure, (2) lowering of standards in other defect categories and (3) actual increased nervous tension among the examined registrants as a result of the entry of the United States into the war and as the war progressed. These factors make it difficult to determine the effect of the changes in the ages of the examined registrants during each of the four years on the rejection rate for mental and personality disorders.[3]

The first two factors, which produced apparent but not real increases, were partially responsible for the

2. Additional data on rejection rates and the prevalence of mental and personality disorders are to be found in the following bulletins published by the Selective Service System: Medical Statistics Bulletin No. 1, Nov. 10, 1941, Medical Statistics Bulletin No. 2, Aug. 1, 1943 and Medical Statistics Bulletin No. 3, Nov. 1, 1944.

3. During 1940 and 1941 the majority of examined registrants were in the age group 21-35; in 1942 the age group was enlarged to 20-44; in 1943 and 1944 only registrants aged 18-37 were examined. During 1944, however, the average age of the examined registrants was lower than in 1943.

increase in the rate from 1940-1941 to 1942. During peacetime most of the registrants who were rejected were examined only by the general practitioner giving the local board examination, and comparatively few rejections were made for mental and personality disorders. Beginning in 1942 the local board physician gave only a screening examination, and most of the rejections were made after the induction station examination, which included an interview with a psychiatrist. The result was that the psychiatrist diagnosed many cases of mental and personality disorders which probably would have been missed by the general practitioner.

The second factor, the lowering of standards in other defect categories, operated with the first to produce an apparent increase in rejections for mental and personality disorders. Thus during peacetime tooth and eye standards were very high and tooth and eye defects were the leading causes for rejection. With the lowering of tooth and eye standards in 1942 the probability of being rejected for mental and personality disorders increased, since many registrants who would have been rejected for the more obvious tooth or eye defects also had mental and personality disorders of a disqualifying nature.

The third factor, increased nervous tension of registrants after the entry of the United States into the war, was partially responsible for the pronounced rise in the rejection rate for mental and personality disorders from 1942 through 1944. How much of the rise is due to this third factor is difficult to evaluate because of the changes in physical standards in other defect categories and the variations in the application and interpretation of the standards for mental and personality disorders. As the war progressed there was also the possibility that within the extremely limited time allotted for the psychiatric interview and the increasing efforts of the armed forces to maintain at a minimum discharges for psychiatric reasons, some psychiatrists may have been overcautious in excluding borderline cases from the armed forces.

For both races, rejection rates for mental and personality disorders increased with each succeeding year; the rate for Negroes increased more rapidly than for white registrants. In 1940-1941 and 1942 the Negro rates were 40 per cent and 60 per cent as great as the white rates. In 1943 and 1944 the rates for the two races were approximately equal. This greater increase for Negroes is mainly attributable to the fact that beginning in 1943 a greater proportion of Negroes were examined by psychiatrists than in 1942, as a result of the relaxed venereal standards.[4]

MAJOR SUBGROUPS OF MENTAL AND PERSONALITY DISORDERS

This section deals with the occurrence of the major subgroups of mental and personality disorders among all examined registrants whether or not they were rejected and as causes for rejection among rejected registrants only. The prevalence data afford a more nearly complete picture of the disorders than data on causes for rejection, since (1) in some cases registrants with mild mental or personality disorders such as transient psychoneurosis because of anxiety over the outcome of the examination were found acceptable for service if otherwise physically fit and (2) some registrants with both physical defects and mental and personality disorders were rejected primarily for physical defects and hence would not be counted in the rejections.[5]

During 1940 and 1941 approximately 26 out of every thousand white registrants examined were recorded as having some form of mental or personality disorder, while for Negroes the defect was found one third as often (table 3). Psychoneurotic disorders were the most frequent type of disorder recorded for both races—the bases for more than half of these diagnoses were functional disorders of expressive movements (tics, stammering, stuttering) and neurocirculatory asthenia. The prevalence rate for this defect among white registrants was more than four times that for Negroes. Psychopathic personality was next in order of importance, but the white rate was only twice the Negro rate.

TABLE 2.—*Estimated Rejection Rates for Mental and Personality Disorders by Race, 1940-1944* *

Year	All Races	White †	Negro
1940-1941	22.3	24.5	9.9
1942	49.6	52.4	32.4
1943	73.7	73.8	73.0
1944	120.2	119.3	126.7

* Rate per thousand examined.
† Includes all races other than Negro.

TABLE 3.—*Prevalence of Mental and Personality Disorders and Percentage Distribution of Rejections for These Defects Among Registrants Physically Examined at Local Boards, 1940-1941* *

Major Subgroup	Prevalence per 1,000 Examined			Per Cent Distribution of Rejections		
	All Races	White †	Negro	All Races	White †	Negro
Total	23.7	25.7	7.8	100.0	100.0	100.0
Grave mental or personality disorders	1.6	1.8	0.5	13.5	13.6	11.6
Major abnormalities of mood	0.6	0.6	0.2	3.1	3.1	1.9
Psychopathic personality	2.7	2.8	1.7	11.3	10.9	19.2
Psychoneurotic disorders	14.9	16.3	3.7	49.2	49.8	34.6
Chronic inebriety and drug addiction	1.5	1.6	0.7	5.9	5.7	9.6
Mental and personality disorders not classifiable elsewhere	2.4	2.6	1.0	17.1	16.9	23.1

* Corresponding data for induction stations are not available for the period 1940-1941.
† Includes all races other than Negro.

Studies made on obvious defects indicate that slightly less than one half of those diagnosed as having grave mental or personality disorders had been treated in hospitals for the mentally ill. In other words, the basis for the diagnoses in many of those "obvious" cases was an affidavit from a physician or a mental hospital.

Statements of institutional treatment for unspecified mental conditions and indefinite descriptions of mental or personality disorders are included in the subdivision "Mental and Personality Disorders Not Classifiable Elsewhere." More than one half of those so classified had "obvious" defects and in all likelihood had either a manic-depressive psychosis or schizophrenia or a history of one of these conditions.

The importance of the various subgroups as causes for rejection at local boards as shown in table 3 reveals that almost one half of the rejections were due to psychoneurotic disorders; the next largest groups were

4. In 1942 syphilis was the leading cause for rejection among Negroes, and the great majority of these rejections were based on local board screening examinations. During 1943 registrants with venereal diseases were inductible into the armed forces, so that registrants with these defects were forwarded to induction stations, where they received a psychiatric examination as part of the induction station routine.

5. Methods used in selecting the principal cause for rejection are explained in Edwards, T. I., and Hellman, L. P.: Methods Used in Processing Data from the Physical Examination Reports of the Selective Service System, J. A. Statistical A. **39**: 165-182 (June) 1944.

mental and personality disorders not classifiable elsewhere and grave mental or personality disorders. Psychopathic personality ranked fourth in importance as a cause for rejection, in contrast to second place as a recorded defect among all examined registrants.

Psychoneurotic disorders accounted for only one third of the Negro rejections for mental and personality disorders, in contrast to one half for white registrants. A higher proportion of Negro than white rejections were for mental and personality disorders not classifiable elsewhere, psychopathic personality and chronic inebriety and drug addiction. In the case of psychopathic personality, particularly, the proportion of rejections for this defect among Negroes was twice as great as that among white registrants.

The prevalence of mental and personality disorders during 1942 and 1943 was 67.5 per thousand registrants examined (table 4). They were diagnosed relatively more frequently among white registrants than among Negroes. Psychoneurosis and psychopathic personality were the most frequently recorded mental and personality disorders. Psychopathic personality was the only subgroup which was recorded relatively more often for Negroes than for white registrants. The other specific mental and personality disorders, of a more serious nature, were found only one third as often among Negroes as among white registrants.

Psychoneurosis was the most frequent cause for rejection for mental and personality disorders among both races during 1942 and 1943, with psychopathic personality next in importance. Among white registrants, psychoneurosis accounted for twice as many rejections as psychopathic personality. Both defects were equally important as causes for rejection of Negroes, accounting for 9 out of every 10 rejections for mental and personality disorders. Grave mental or personality disorders, although next in importance, accounted for relatively few rejections among both races.

TABLE 4.—*Prevalence of Mental and Personality Disorders and Percentage Distribution of Rejections for These Defects Among Registrants Physically Examined at Local Boards and Induction Stations, 1942-1943*

Major Subgroup	Prevalence per 1,000 Examined			Per Cent Distribution of Rejections		
	All Races	White*	Negro	All Races	White*	Negro
Total	67.5	70.6	50.3	100.0	100.0	100.0
Grave mental or personality disorders	5.6	6.3	2.1	8.2	8.7	4.6
Major abnormalities of mood	1.2	1.3	0.2	2.1	2.2	0.8
Psychopathic personality	18.2	17.6	21.5	29.3	27.1	44.9
Psychoneurotic disorders	37.0	39.3	24.1	54.3	55.5	46.2
Chronic inebriety and drug addiction	4.0	4.5	1.1	4.3	4.7	1.8
Mental and personality disorders not classifiable elsewhere	1.5	1.6	1.3	1.8	1.8	1.7

* Includes all races other than Negro.

THE AGE FACTOR

In general, it can be stated that with increasing age the rejection rate for mental and personality disorders increased. However, the specific diagnoses differed in importance as causes for rejection when considered in relation to age. During 1944 the three leading diagnoses of mental and personality disorders were psychoneurosis, emotional instability and asocial and amoral trends. In addition, for the 18 year olds, emotional immaturity was one of the more important diagnoses.[6] The distribution of these diagnoses in relation to total mental and personality disorder rejections by age is shown in table 5.

The importance of psychoneurosis as a cause for rejection increased with increasing age—out of every hundred 18 year olds rejected for mental and personality disorders approximately 30 were rejected for psychoneurosis, whereas the corresponding number among those 30 years of age and over was approximately 65. For emotional instability the situation was just the reverse—relatively more of the younger registrants rejected for mental and personality disorders had emotional instability diagnosed than the older registrants. With respect to asocial and amoral trends, relatively more of the rejections occurred among those under 25 than among those 25 and over. Emotional immaturity was the second leading diagnosis of mental and personality disorders among the 18 year olds, accounting for over one fifth of the mental rejections. As would be expected, its importance was negligible for those over 19 years of age. These age trends held for white registrants. Among Negroes, however, the only distinct age trends were for psychoneurosis and emotional immaturity.

TABLE 5.—*Percentage of Mental and Personality Disorder Rejections Due to Selected Diagnoses, by Age* **

Age	Total	Psychoneurosis	Emotional Instability	Asocial and Amoral Trends	Emotional Immaturity	Other Mental
			All Races			
All ages	100.0	59.1	20.3	11.4	2.5	6.7
18	100.0	30.3	24.3	11.9	22.7	10.8
19	100.0	42.2	25.8	11.2	8.9	11.9
20-24	100.0	56.1	22.1	13.0	0.4	8.4
25-29	100.0	64.0	19.6	10.9	†	5.5
30-37	100.0	64.7	18.8	10.9	†	5.6
			White ‡			
All ages	100.0	62.5	19.0	9.3	2.8	6.4
18	100.0	31.1	24.0	9.8	25.1	10.0
19	100.0	44.6	24.5	8.5	9.9	12.5
20-24	100.0	60.5	21.0	10.2	0.5	7.8
25-29	100.0	68.2	18.0	8.6	†	5.2
30-37	100.0	67.8	17.5	9.2	†	5.5
			Negro			
All ages	100.0	35.6	29.4	25.8	0.9	8.3
18	100.0	25.3	26.3	25.0	7.1	16.3
19	100.0	28.7	32.8	26.4	3.4	8.7
20-24	100.0	34.5	28.0	26.9	...	10.6
25-29	100.0	36.8	30.5	26.4	0.1	6.2
30-37	100.0	38.9	30.2	24.9	...	6.0

* Based on a sample of Reports of Physical Examination and Induction for registrants inducted or rejected during February 1944-May 1944.
† Less than 0.05 per cent.
‡ Includes all races other than Negro.

Emotional immaturity and psychoneurosis accounted for a larger proportion of the mental rejections among white registrants, age for age, than among Negroes, while the reverse was true for emotional instability and asocial and amoral trends. The difference between the races was more pronounced with respect to asocial and amoral trends than for emotional instability.

THE OCCUPATIONAL FACTOR

The relationship of occupation and rejections for mental and personality disorders is shown in table 6. In evaluating these data it should be borne in mind that Selective Service policies with regard to occupational deferment have resulted in physical examination of relatively fewer men in some occupational groups than

6. Data on mental and personality disorders of 18 and 19 year old registrants examined during December 1942-February 1943 are included in Rowntree, L. G.; McGill, K. H., and Edwards, T. I.: Causes of Rejection and Incidence of Defects Among 18 and 19 Year Old Registrants, J. A. M. A. **123**: 181-185 (Sept. 25) 1943.

in others, and that, therefore, the occupational groups vary in their representativeness with respect to physical or mental condition. The farm group is probably the least representative of their group in the general population, owing to the passage of the Tydings Amendment, which deferred certain classes of agricultural workers. At the other extreme are the clerical, sales and service workers, and the emergency workers and unemployed.

Rejections for mental and personality disorders were highest among farmers and farm managers (143.4 per thousand examined) and emergency workers, unemployed and nonclassifiable (142.5). Students had the lowest rejection rate for this condition (72.9). The low rejection rate for students is probably due to their youth more than to any other factor.

Psychoneurosis rejection rates were highest for the professional and managerial and lowest for students. Farmers and farm managers had a rate 50 per cent higher than that for farm laborers. Rejections for reasons other than psychoneurosis were highest for the emergency workers, unemployed and nonclassifiable and lowest for professional and managerial. It can also be noted that farm laborers, students and emergency workers, unemployed and nonclassifiable were less apt to be rejected for psychoneurosis than for other mental conditions, which consist mainly of emotional instability and asocial and amoral trends, and that the reverse was true for all other occupations. In addition, a comparison of the rejection rate for craftsmen with that for operatives and laborers reveals a higher rejection rate for psychoneurosis and a lower rate for other mental disorders among the skilled workers than among the semiskilled and unskilled.

If only gainfully employed workers are considered (thus excluding students and the emergency worker group) it can be seen that professional and managerial workers had the highest psychoneurosis rejection rate and the lowest rate for all other mental conditions, while farm laborers had the lowest rate for psychoneurosis and the highest for all other mental conditions.

TABLE 6.—*Rejection Rates for Mental and Personality Disorders per Thousand Registrants Examined, by Occupation* *

Occupation	Total	Psychoneurosis	Mental and Personality Disorders Excluding Psychoneurosis
All occupations	113.1	63.0	50.1
Professional and managerial	109.9	85.2	24.7
Farmers and farm managers	143.4	80.9	62.5
Clerical, sales and service workers	106.4	67.9	38.5
Craftsmen	109.4	71.5	37.9
Operatives and laborers, except farm	111.0	60.6	50.4
Farm laborers	118.7	53.8	64.9
Students	72.9	32.1	40.8
Emergency workers, unemployed and nonclassifiable †	142.5	57.7	84.8

* Based on a sample of Reports of Physical Examination and Induction for registrants examined during November 1943-December 1943.
† Nonclassifiable constitute a negligible proportion of this group.

MEDICAL SURVEY PROGRAM

During the operation of the Selective Service System much information has been been provided by the system bearing on the mental and personality status of registrants. This information has furnished the basis in many instances for acceptance or rejection of registrants by the armed forces. Prior to Oct. 4, 1943 many of the states developed some plan for obtaining medical and social histories of each registrant facing induction. On Oct. 4, 1943 a Medical Survey Program was initiated by the Selective Service System to coordinate and unify procedures for obtaining (1) additional medical and social histories on registrants classified or about to be classified into a class immediately available for service and (2) education histories from secondary schools for potential registrants 15 years of age and over and registrants classified or about to be classified into a class immediately available for service.[7]

Salient features of the medical survey program include (1) appointment on a voluntary basis of one or more persons in each local board area who are qualified to do health or social work as medical field agents and (2) procurement by the state director of educational histories of registrants for use by the induction stations. The medical field agents obtain medical and social histories of registrants from such sources as the registrant's personal physician, social service exchanges, hospitals and clinics and correctional institutions or agencies. At present there are more than 9,000 medical field agents, and medical survey information is being supplied for a substantial percentage of the registrants considered for induction.

SUMMARY

A review of prevalence and rejections for mental and personality disorders among Selective Service registrants shows that:

1. The majority of rejections for mental and personality disorders were made by armed forces' psychiatrists; these rejections were made on the basis of unfitness for military life, although not all the disorders were handicapping in civilian life.

2. Mental and personality disorders were the principal cause for rejection of 801,700, or approximately 17.8 per cent, of registrants aged 18-37 in rejected classes on Jan. 1, 1945.

3. The rejection rate for this type of disorder increased from 22.3 per thousand examined in peacetime to 120.2 per thousand examined in 1944.

4. The rise in the rejection rate was not solely due to increased nervous tension among examined registrants. Other factors to be considered are changes in examining procedure, lowering of standards in other defect categories and stricter interpretation of standards for mental and personality disorders by the armed forces' psychiatrists.

5. Relatively more white registrants than Negroes have been rejected for mental and personality disorders.

6. Psychoneurotic disorders and psychopathic personality account for more than 8 out of every 10 rejections for mental and personality disorders.

7. Psychopathic personality is more prevalent among Negroes than among white registrants, while the reverse is true for psychoneurosis.

8. With increasing age, relatively more registrants are rejected for psychoneurotic disorders.

9. Among 18 year olds more than one fifth of the rejections for mental and personality disorders are due to emotional immaturity.

10. Of those gainfully employed, the psychoneurosis rejection rate was highest for professional and managerial workers and lowest for farm laborers, while the rate for other mental and personality disorders (consisting mainly of emotional instability and asocial and amoral trends) was lowest for the former and highest for the latter.

7. Full details are given in Medical Circular No. 4, issued by the Selective Service System on Oct. 18, 1943.

THE USE OF FIBRIN FILM AS A DURAL SUBSTITUTE

AND IN THE PREVENTION OF MENINGOCEREBRAL ADHESIONS

FURTHER STUDIES AND CLINICAL RESULTS

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The need for a material which acts as a substitute for excised or injured dura mater and at the same time prevents meningocerebral adhesions has long been one of the most pressing in neurologic surgery. Numerous dural substitutes have been tried with varying degrees of success. On long-range study not one has proved adequate to fill these requirements.[1] In spite of this, the results secured when no material is employed have been so unsatisfactory that most neurosurgeons prefer to use one or another of the available dural substitutes, whatever their shortcomings may be.

In the course of a program devoted to the fractionation of human blood plasma,[2] large quantities of human

Fig. 1.—Dry fibrin film after removal from the glass ampule.

fibrinogen and thrombin have become available.[3] From these proteins it has been possible to prepare a material, fibrin film,[4] which has been subjected to experimental and clinical trial as a dural substitute.[5]

A variety of films may be prepared from solutions of thrombin and fibrinogen by varying the conditions under which clotting takes place and by changing the amount and character of the plasticizer present.[4] One type has been selected as most suitable as a dural substitute in physical properties and tissue reactions. It has been prepared with a low water content, so

Fig. 2.—Fibrin film after soaking in saline solution for fifteen minutes. It has become flexible and is easily handled.

that it can safely be used a long time after distribution.[6] In this state fibrin film is translucent, firm and somewhat brittle when dry (fig. 1). After immersion in saline solution for fifteen minutes the physical properties are once more those of a moist membrane. The wet film is almost transparent but has become flexible (fig. 2) and elastic, returning to its original size and shape when stretched for 100 per cent of its length (fig. 3). Microscopic study of the fibrin film shows that it consists of a uniform sheet without interstices visible with oil immersion lenses. Diglycine passes through steam-sterilized fibrin film but hemoglobin does not.[7]

As prepared for distribution, fibrin film is packaged dry in a glass ampule (fig. 4). Sterilization has been

Fig. 3.—Fibrin film is elastic.

carried out in the ampule, and the fibrin film may not be resterilized.

From the Surgical Services of the Children's Hospital and the Peter Bent Brigham Hospital and from the Departments of Surgery and Pathology of the Harvard Medical School.

This work has been carried out under contract recommended by the Committee on Medical Research between the Office of Scientific Research and Development and Harvard University.

This paper is No. 37 in the "Studies of Plasma Proteins" of the Harvard Medical School, Boston, on products developed by the Department of Physical Chemistry from blood collected by the American Red Cross.

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3. Edsall, J. T.; Ferry, R. M., and Armstrong, S. H., Jr.: Chemical, Clinical and Immunological Studies on the Products of Human Plasma Fractionation: XV. The Proteins Concerned in the Blood Coagulation Mechanism, J. Clin. Investigation **23**: 557-565, 1944.

4. Ferry, J. D., and Morrison, P. R.: Chemical, Clinical and Immunological Studies on the Products of Human Plasma Fractionation: XVI. Fibrin Clots, Fibrin Films and Fibrinogen Plastics, J. Clin. Investigation **23**: 566-572, 1944.

5. Bailey, O. T., and Ingraham, F. D.: Chemical, Clinical and Immunological Studies on the Products of Human Plasma Fractionation: XXII. Fibrin Films in Neurosurgery, with Special Reference to Their Use in the Repair of Dural Defects and in the Prevention of Meningocerebral Adhesions, J. Clin. Investigation **23**: 597-600, 1944. Ingraham and Bailey.[5]

6. Physical and chemical studies leading to the development of the present product, which is steam sterilized in the final containers before distribution, have been carried out by Dr. J. D. Ferry and Mr. P. R. Morrison in the Department of Physical Chemistry, Harvard Medical School, in collaboration with Drs. J. D. Porsche and R. L. Kutz of the Armour Laboratories under contract recommended by the Committee on Medical Research between the Office of Scientific Research and Development and Harvard University.

7. Ferry, J. D., and Morrison, P. R.: Personal communication to the authors.

ANIMAL EXPERIMENTS

When fibrin film first became available for trial as a dural substitute, sterilization was carried out in glycerol, a procedure practical on a small scale in the laboratory but cumbersome in large-scale production. Experiments with these films have been reported in detail elsewhere.[8]

After trying various methods of sterilization, it was found possible to sterilize fibrin film in the final container by steam under pressure.[8] Although films treated in this way were similar in physical properties to the glycerol-sterilized films, it seemed advisable to repeat the experimental studies before using steam-sterilized fibrin films on human patients.

The following procedure was carried out on 15 monkeys (Macaca mulatta):

After shaving the scalp, the field was cleansed with alcohol and zephiran. A midline incision was made in the scalp and a large temporoparietal decompression was performed on each side of the skull with sacrifice of the bone. On the left, a circular area of dura approximately 1.2 cm. in diameter was removed. A piece of fibrin film slightly larger than the dural defect (about 1.5 cm. in diameter) was placed over the intact arachnoid, the excess film being placed under the edges of the dura without suture. On the right the same

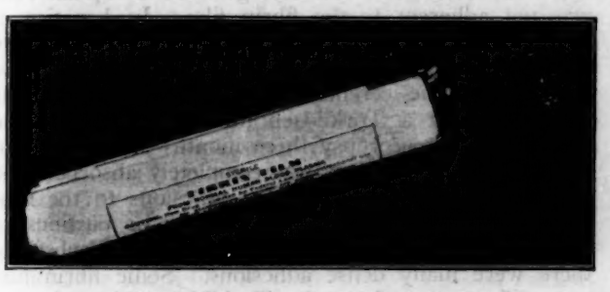

Fig. 4.—Unopened ampule of fibrin film.

procedure was carried out with the variation that in several areas a curved French needle was inserted through the leptomeninges into the outer layers of the cerebral cortex and then pulled out so as to lacerate the arachnoid, pia and the superficial cerebral tissues. The temporal muscles were closed over the fibrin films on both sides and the superficial tissues sutured with black silk.

The monkeys were killed at intervals of one day, two weeks and one, two, three, five and six months after operation. No abnormalities were noted in any of the monkeys during the survival period.

Pathologic studies indicated that the fibrin films were gradually replaced by a neomembrane of fibrous tissue without the formation of meningocerebral adhesions. In a few of the monkeys the fibrin film had slipped somewhat, so that a portion of the dural defect was covered by fibrin film and the rest by temporal muscle. Adhesions formed between the muscle and the arachnoid but did not form between the fibrin film and the arachnoid. Absorption of the fibrin film was almost complete at three months, and no film remained at five and six months after operation (fig. 5). The histologic sequences involved in the replacement of the steam-sterilized fibrin films were identical with those induced by glycerol-sterilized films; these have been discussed elsewhere.[8]

These experimental studies indicated that fibrin film as now distributed was safe for clinical trial as a dural substitute and in the prevention of meningocerebral

Fig. 5.—Brain of monkey six months after the use of fibrin film as a dural substitute. Note the absence of adhesions and the normal appearance of the cortical structures. At the right is the portion of dura in which a circular defect was covered by fibrin film. The neomembrane replacing the fibrin film blends with the dura and is almost indistinguishable from it.

adhesions. They also suggested that the experience gained from the use of the original films was applicable to the present material.

CLINICAL STUDIES

The clinical evaluation of any new material for use as a dural substitute is exceedingly difficult. Of the numerous substances suggested from time to time, experience has shown that favorable results may be obtained in a series of patients, only to be followed by untoward sequelae in other patients as the series is extended, or by late complications when the result had appeared at first satisfactory.[1]

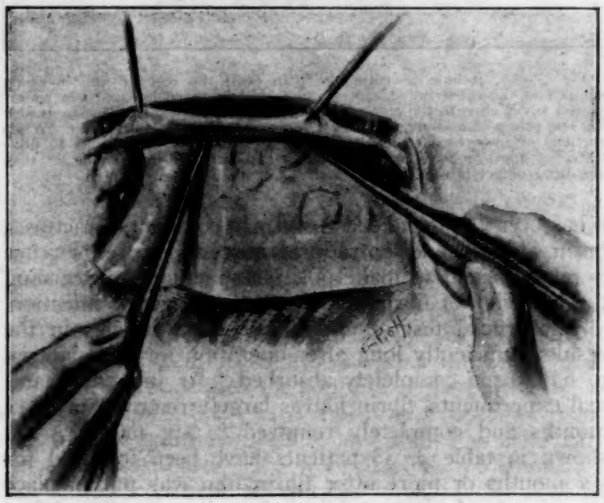

Fig. 6.—Technic used to hold the fibrin film in place without sutures. Although a portion of the cortex is shown uncovered by film in the drawing, a piece of fibrin film larger than the defect is used in the operation.

We have attempted to evaluate fibrin film as a dural substitute in the following ways: (1) by using it in as large a series of patients as possible, (2) by making use of it in many different types of neurosurgical procedures, (3) by following the patients until the fibrin film has been absorbed and (4) by studying

8. Ingraham, F. D., and Bailey, O. T.: The Use of Products Prepared from Human Fibrinogen and Human Thrombin in Neurosurgery: Fibrin Foams as Hemostatic Agents; Fibrin Films in Repair of Dural Defects and in Prevention of Meningocerebral Adhesions, J. Neurosurgery 1: 23-39, 1944.

the films or regions in which they have been used at secondary operations or at necropsy. This report is based wholly on our personal experience.

The glycerol-sterilized films have been used as dural substitutes in 59 neurosurgical procedures and the steam-sterilized films in 35. Since the animal experiments suggest that the tissue reactions of the two types of films are very similar, it may be permitted to combine these figures, giving a total series of 94 instances in which fibrin film has been employed by us as a dural substitute and for the prevention of meningocerebral adhesions. This series would seem sufficiently large to give a definite indication of the advantages and limitations of the material.

Furthermore, the neurosurgical procedures have been carried out in the treatment of a variety of lesions (table 1) and in different regions of the central nervous system (table 2). They include operations for tumors of the brain and spinal cord, congenital malformations, degenerative diseases and traumatic lesions. The results have been uniformly favorable, regardless of the nature of the lesion which made advisable the use of a dural substitute. It should be pointed out that in the large majority of the patients fibrin film was used in a presumably sterile operative field. While

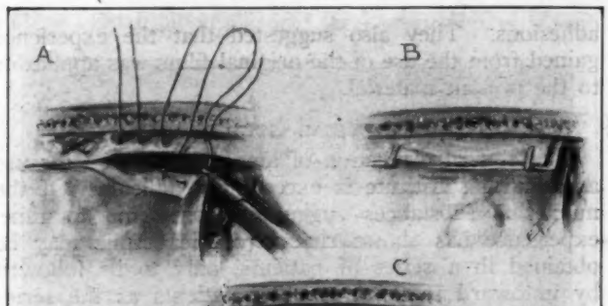

Fig. 7.—*A*, technic of suturing fibrin film; the cuff of film is easily sutured to the overlying dura. *B*, film held in place by applying widely spaced silver clips to the cuff. *C*, the fibrin film is held in place by inserting one prong of a silver clip through an opening in the fibrin film. While portions of uncovered cortex are shown in each of the drawings to illustrate the appearance of a cross section, a piece of fibrin film larger than the dural defect is used in the operating room.

it has been employed successfully in compound fractures, brain abscess and extradural abscess, our experience is not sufficient to make positive statements concerning the behavior of fibrin film in the presence of infection.

The crucial test of any dural substitute lies in the results sufficiently long after operation for the material to have been completely absorbed. As judged by animal experiments, fibrin film is largely removed in three months and completely removed in six months. As shown in table 2, 33 patients have been followed for six months or more after fibrin film was put in place as a dural substitute. All of them have remained free from symptoms referable to the fibrin film; in not a single instance have untoward sequelae developed. Furthermore, it has been evident that there was less cortical irritation as the result of the pathologic lesions present than would have been expected if no protective covering had been used.

As a final criterion, attempts have been made to study at secondary operation or at necropsy the site in which fibrin film had been placed. This has been possible in 19 patients in whom glycerol-sterilized fibrin film had been used, the times varying from fourteen hours to eighty-one days. The site of operation has also been studied a few hours to three months later in 8 instances in which steam-sterilized fibrin film had been left in place. Those recovered within two months after operation showed little change from their original appearance, and the underlying brain or spinal cord was not adherent to the fibrin film. In 1 patient a piece of steam-sterilized film was used to cover a large suboccipital defect created in an operation for medulloblastoma of the cerebellum, and another piece was wrapped about a Torkildsen tube put in during the procedure. At necropsy three months later the fibrin film over the cerebellum was completely absorbed; the arachnoid was smooth without adhesions to the neomembrane replacing the fibrin film. In portions of the operative field not covered by a dural substitute there were many dense adhesions. Some fibrin film was still present about the Torkildsen tube. It was thinner than it was at the time of operation but otherwise was unchanged in appearance and was not adherent to adjacent structures.

TABLE 1.—*Lesions Treated*

Diagnosis	Total Number	Glycerol Sterilized Film	Steam Sterilized Film	Duration <6 Mos.	Duration >6 Mos.
Skull fracture	5	3	2	3	2
Subdural hematoma	2	1	1	1	1
Jacksonian epilepsy	4	3	1	1	3
Brain abscess	2	1	1	2	0
Extradural abscess	1	1	0	0	1
Tuberculous meningitis	2	2	0	2	0
Chronic arachnoiditis	1	1	0	1	0
Encephalitis	1	0	1	1	0
Chronic progressive encephalopathy	2	1	1	2	0
Lead encephalitis	6	6	0	4	2
Arnold Chiari malformation	4	3	1	3	1
Spina bifida and cranium bifidum	9	3	6	6	3
Scaphocephaly	4	1	3	3	1
Hydrocephalus	9	5	4	6	3
Tumors of brain and spinal cord	42	28	14	26	16
Total cases	94	59	35	61	33

TABLE 2.—*Location of Lesions*

Type of Film	Region	Total	Duration <1 Mo.	1-6 Mo.	6-12 Mo.	12-18 Mo.	18-24 Mo.
Glycerol sterilized	Frontal	6	1	1	0	2	2
	Parietal	22	8	3	2	5	4
	Temporal	14	5	2	0	2	5
	Occipital	3	1	1	0	1	0
	Posterior fossa	8	4	1	1	0	2
	Cervical cord	2	1	0	0	0	1
	Thoracic cord	3	0	1	0	0	2
	Lumbar cord	1	0	0	0	0	1
Steam sterilized	Frontal	5	1	4	0	0	0
	Parietal	3	1	1	1	0	0
	Temporal	8	1	7	0	0	0
	Posterior fossa	16	4	10	2	0	0
	Lumbar cord	3	0	3	0	0	0
Total		94	27	34	6	10	17

In view of these experiences, it would appear that fibrin film is the most satisfactory material now available for use as a dural substitute and in the prevention of meningocerebral adhesions.

TECHNICAL CONSIDERATIONS

Fibrin film is packaged in a glass tube (fig. 4), which should be kept in an ice box if possible, though it may be left at room temperature for many weeks without detectable evidence of deterioration. When

it is to be used as a dural substitute, the outside of the tube is sterilized by soaking in alcohol or other germicide. The tube is then washed with cool sterile saline solution (i. e. at room temperature) to remove any adherent germicide. The constricted band on the tube is scored with a file and the top struck sharply. Before the film is removed, the tube is filled with cool sterile saline solution and allowed to soak fifteen minutes. This is important because the film is brittle and difficult to handle when dry. After soaking, the film and paper wrapped about it are removed together by means of forceps. The paper is discarded and the film is immersed in cool saline solution until it is required. The film should not be allowed to dry at any time and must be kept well moistened even in the operative field. It should be used the same day the tube is opened.

At operation a piece is cut from the fibrin film corresponding in shape to the dural defect and somewhat larger than it. In the majority of instances it is not necessary to secure the fibrin film in place. A satisfactory result is obtained merely by placing the edges of the fibrin film carefully under the cut edge of the dura (fig. 6). When dealing with a small defect or one in which the surgeon for any reason is concerned about displacement of the fibrin film, its position can be maintained by carefully placed mattress sutures. This procedure is best carried out by folding the edge and suturing the cuff thus obtained (fig. 7 *A*). A cuff of the fibrin film may also be affixed to the dura by widely placed silver clips (fig. 7 *B*). An alternative method is to make a small opening in the fibrin film and to insert one prong of a silver clip through it (fig. 7 *C*). If sufficient care is used and the film is kept moist, the material is not difficult to suture or to clip, but if it is allowed to dry it is almost impossible to hold the fibrin film in place by any fixation method. It should be emphasized that instances requiring sutures or silver clips to hold the fibrin film in place are rare; in most instances, tucking an edge of the fibrin film under the dura gives the best results.

After the fibrin film is in place, the wound is closed by the same technic which would have been used had no dural substitute been employed.

COMMENT

Fibrin film has been shown to have the physical properties desirable in a dural substitute. In monkeys it not only leads to the formation of a neomembrane which forms a satisfactory protective covering but it also prevents the formation of meningocerebral adhesions. A thorough clinical trial indicates its safety and value in many locations and in the treatment of a variety of lesions.

While dural substitutes are required in a relatively small percentage of peacetime neurosurgical procedures, the situation is different in military neurosurgery. Reports indicate that the necessity of a dural substitute in head wounds is so great that the available materials, such as fascia lata and preserved human dura, are used even by those neurosurgeons who are well aware of the fact that the materials produce widespread meningocerebral adhesions. This is because they feel that the late clinical complications would be even more severe if no dural substitute was employed. These facts indicate that any dural substitute better than fascia lata or preserved human dura could be used by the armed forces to advantage.

The clinical and experimental studies of fibrin film show that it has great advantages over any other dural substitute now available. In addition it is prepared on a large scale; it is stable at ice box temperature for over a year and at room temperature for many months; it is easy to use in the operating room. It is still far too soon to assert that fibrin film is the ideal dural substitute; it does not seem too soon to state that it has important advantages over other dural substitutes now available.

SUMMARY

Fibrin film, prepared from human fibrinogen and thrombin, is now available for use as a dural substitute and in the prevention of meningocerebral adhesions.

Clinical and experimental studies indicate that it has many advantages over other dural substitutes now available.

300 Longwood Avenue.

TRANSFUSION OF O BLOOD

CONDITIONED BY THE ADDITION OF BLOOD GROUP SPECIFIC SUBSTANCES

FURTHER CLINICAL INVESTIGATIONS

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AND
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Group O blood has been used extensively as universal blood. Carefully investigated reactions to group O blood, published by workers with extensive experience in the field of blood transfusion, have caused many physicians to object to this method as a general procedure, granting that the Rh factor is given proper consideration as a source of reactions. It is reasonable to assume that isoagglutinins introduced into the circulation of human beings harboring the corresponding agglutinogens in the cells and plasma should combine with both, and it is a surprising fact that damaging reactions are not observed more frequently. Aubert, Boorman and Dodd [1] have demonstrated the occurrence of intravascular agglutination and hemolysis in a significant percentage of cases following the transfusion of serum of group O into recipients belonging to group A. On the basis of such observations the indiscriminate use of universal blood for transfusions into patients of different blood groups does not appear to us to be a recommendable procedure at present.

To overcome the objections to the use of group O blood with potent isoagglutinins as a universal blood, we have recommended the addition of the purified blood group specific substances A and B as a means of reducing the isoagglutinin titers to low levels.[2] In our early series of 147 cases [3] we were unable to demonstrate any untoward effect attributable to the addition of the blood group specific substances. A few of these patients received several transfusions at intervals of from ten days to three weeks.

From the Buffalo General Hospital and the Department of Bacteriology and Immunology, University of Buffalo School of Medicine.

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2. Witebsky, E.; Klendshoj, N. C., and Swanson, P.: Preparation and Transfusion of Safe Universal Blood, J. A. M. A. **116**: 2654 (June 14) 1941.
3. Klendshoj, N. C.; McNeil, C.; Swanson, P., and Witebsky, E.: Transfusion of Conditioned Universal Blood, Arch. Int. Med. **70**: 1 (July) 1942.

To give further consideration to the problem of safety in conditioning of O blood with blood group specific substances, we have compared an additional series of 389 transfusions of O blood containing the purified group specific substances with 1,830 transfusions of homologous blood (belonging to the same blood group as the patient's blood) given under identical conditions. We added 5 to 10 cc. of a previously standardized solution of the blood group specific substances [4] to each pint of O blood either immediately before the transfusion was given or at the time the blood was made available for storage in the blood bank. The 389 transfusions of universal blood, conditioned by the addition of the A and B substances, were given without selection to recipients of all blood groups, frequently as an emergency procedure to avoid loss of time in typing and cross matching. We also prefer this method outside regular laboratory hours, as it eliminates the dangers inherent in blood matching by interns with limited experience in such work. Regarding specific technic, we refer to previous publications.[5]

Distribution of Reactions

Type of transfusion	Homologous		"Conditioned" Universal	
Total number of transfusions	1,830		389	
Reactions	No.	%	No.	%
Pyrogenic				
Grade 1	18	1	0	0
Grade 2	12	0.7	4	1
Grade 3	50	2.7	10	2.6
Hemolytic	5	0.3	0	0
Allergic	28	1.5	5	1.3
Circulatory	3	0.2	0	0
Undetermined	3	0.2	0	0
Total number of reactions	119	6.5	19	4.9

We have established a definite routine to secure recording of sufficient data for every transfusion on which classification of transfusion reactions may be based. For this purpose a special transfusion sheet is filled out by the house physician in charge of the transfusion and by the assisting nurse. Frequent determinations of temperature, pulse rate and blood pressure over a period of six to eight hours following transfusion are requested. In case of a reaction, determinations of icterus index, quantitative van den Bergh, cell counts and examinations of urine for hemoglobinuria are carried out routinely. The respective blood groups of donor and patient are rechecked and possible interference of the Rh factor is investigated. These determinations enable us in most instances to draw a conclusion as to the likely cause of the reactions.

We classify our transfusion reactions into five major groups according to suspected cause: pyrogenic, hemolytic, allergic, circulatory and undetermined.

Temperature reactions with no other untoward manifestations are recorded in the conventional group of pyrogenic reactions and subdivided into three grades: grade 1, a temperature rise of 1 to 2 degrees, grade 2, a rise of 2 to 3 degrees, and grade 3, a rise in temperature of more than 3 degrees or any reaction with a chill. In febrile cases we have excluded higher than normal temperatures as reactions to transfusions, unless comparison of temperature diagrams over a period of several days preceding and following the transfusion demonstrates definite deviation at the time of the transfusion from the patient's general temperature pattern.

The accompanying table shows the distribution of reactions in two groups: transfusions with homologous blood and transfusions with group O blood "conditioned" by the addition of the blood group specific substances A and B.

Comparison between the group of homologous blood transfusions with that of conditioned universal blood shows reaction rates of probable statistical identity. The hemolytic reactions which occurred only in the "homologous" group require comment. One of these reactions was due to administration of B blood to an O recipient by mistake as the result of an unfortunate similarity of names. The intern recognized his mistake before the transfusion had progressed very far. Of the remaining four hemolytic reactions three occurred in Rh negative patients, and there is good reason to believe that the Rh factor was responsible for these reactions. The ideal universal blood consists, therefore, in Rh negative O blood conditioned by the addition of blood group specific substances.

Isoagglutinin titers have been found to increase in patients following erroneous transfusion of incompatible blood. We have used intravenous injections of the purified blood group specific substances to increase isoagglutinin titers for purposes of producing potent typing serum.[6]

Theoretically the possibility exists that transfusion with "conditioned" universal blood might "sensitize" the patient to subsequent administrations of such blood or that even an initial transfusion of "conditioned" blood might cause untoward effects. It should be remembered that the specific substances A and B are added to O blood for the purpose of neutralizing the corresponding antibodies, and they are thus, presumably at least, partly present in combination with these antibodies. However, a biologic response on the part of the patient to injection of the combination is not necessarily excluded.

Further study of these points may be accomplished by a more detailed analysis of the reactions in the group of 389 conditioned universal blood transfusions, as recorded in the table. A total of 308 transfusions were given to patients who had had no previous exposure to the purified A and B substances. We encountered altogether 14 reactions in this group, distributed as follows: 3 (1 per cent) pyrogenic reactions, grade 2; 7 (2.3 per cent) reactions, grade 3, and 4 (1.3 per cent) allergic reactions. These reaction rates conform within statistical limitations to the general reaction rates for the homologous blood. The remaining 81 transfusions in the group of conditioned universal blood were administered to 48 patients who all had received previous transfusions of blood containing the purified A and B substances. The interval between these transfusions varied from a few days to several months. We encountered 5 reactions in these 81 transfusions corresponding to a total reaction rate of 6.2 per cent. The distribution of these reactions was as

4. Prepared by the Eli Lilly Company.
5. Witebsky, Klendshoj and Swanson.[2] Klendshoj, McNeil, Swanson and Witebsky.[3]
6. Witebsky, E.; Klendshoj, N. C., and McNeil, C.: Potent Typing Sera Produced by Treatment of Donors with Isolated Blood Group Specific Substances, Proc. Soc. Exper. Biol. & Med. 55: 167 (March) 1944.

follows: 1 pyrogenic grade 2, 3 pyrogenic grade 3 and 1 allergic. There are no significant differences in these rates and those obtained during the first transfusion of conditioned universal blood.

COMMENT

The problem of the safety of our transfusion procedure parallels in principle the question of transfusions of pooled plasma versus plasma of heterologous blood groups. Quantitatively the problem may be somewhat different, as the amounts of blood group specific substances we add are presumably large in proportion to the amounts naturally contained in plasma. Levine and State [7] reported that they had observed skin reactions to cutaneous injections of plasma derived from various groups. They attributed positive tests to the interaction of the group specific substances in plasma with the corresponding isoantibodies present in the circulation of the person tested, and they explained reactions following transfusion of plasma into persons exhibiting a positive skin test on the same basis as the skin test. To our knowledge their results have not been corroborated, and the explanation has not been accepted. The allergic nature of certain serum and plasma reactions seems to be satisfactorily explained by recent observations of Maunsell.[8]

SUMMARY

A series of 1,830 blood transfusions was compared with a series of 389 transfusions of group O blood to which group specific substances A and B had been added. Special attention was given to the classification and recording of blood transfusion reactions. In spite of rigid and critical observations, no harmful effect was observed attributable to the group specific substances employed. The addition of the purified specific substances A and B to O blood as a means of reducing the corresponding isoagglutinin titers to a low level can therefore be recommended as a safe and effective procedure.

7. Levine, M., and State, D.: A and B Substances as a Cause of Reactions Following Transfusions, J. A. M. A. **120**: 275 (Sept. 26) 1942.
8. Maunsell, K.: Urticarial Reactions in Desensitization in Allergic Recipients After Serum Transfusions, Brit. M. J. **2**: 236 (Aug. 19) 1944.

The Idea of Big Numbers.—We know that one scientist may be worth ten thousand soldiers. The ancient Romans found it out when they attacked Syracuse in Sicily in 212 B. C. only to have their ships fired by burning glasses, smashed by stones from short and long range catapults, pulled out of the water and overturned by iron beaked cranes. All these fearful engines of war, not to mention such useful machines of peace as the water screw for irrigating land and pumping mines, the cogwheel and pulley for launching ships, were the inventions of an "absent minded" mathematician, Archimedes, who considered them "mere diversions of geometry at play." Whether or not he ran naked from his bath shouting "Eureka (I have found it)" on discovering that cunning goldsmiths had defrauded his relative King Gelon of Syracuse by substituting silver for gold in the king's crown, the fact remains that he did work out the laws of floating bodies and fluid displacement ("Archimedes' principle") on which the disclosure of such fraud depended. Among the other primarily mathematical, but later practical, problems which engaged his interest were the laws of the lever ("Give me a place to stand and I will move the earth") and the theory of big numbers, more important in a billion dollar modern world than when Archimedes anciently discussed it in "The Sand Reckoner."—The Autobiography of Science, edited by Forest Ray Moulton and Justus J. Schifferes, New York, Doubleday, Doran & Co., Inc., 1945.

HYPOPROTHROMBINEMIC ACTION OF QUININE SULFATE

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For some time we have been studying blood prothrombin levels in human beings. It seemed of particular interest to one of us (L. P.) to investigate the effect of certain drugs which are administered prophylactically or therapeutically over long periods on the prothrombin level. Among the most widely used compounds of this type are the antimalarials, and the present paper deals with the effect of quinine on the prothrombin time.

Five normal male subjects ranging in age from 18 to 43 years were chosen. Their nutritional state was satisfactory and they were advised to maintain a well balanced diet. The prothrombin time was normal in all instances. Two to four premedication controls, performed in each case, were in agreement within the range of normal variations. In carrying out the estimations the Page [1] method was used. According to this technic viper venom and calcium chloride are added to plasma obtained by centrifuging the decalcified venous blood. The very sharp end point is characterized by the formation of fibrin particles clearly visible in the agitated test tube.

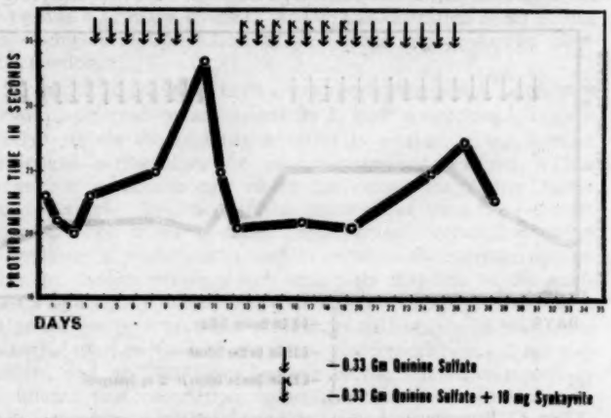

Chart 1.—Representative effects of quinine sulfate on prothrombin time and protective action of vitamin K in S. S., a white man aged 33. In this chart and in chart 2 it is shown that quinine sulfate produces prolongation of the prothrombin time; concurrent vitamin K administration counteracts quinine-induced prothrombinopenia; continuation of quinine sulfate without vitamin K causes another rise of the prothrombin time.

Quinine sulfate in single daily doses of 0.33 Gm. (5 grains) was administered by mouth for periods varying from six to sixteen days. One subject received 0.3 Gm. during the first phase of observation. In all subjects there was a significant rise of the prothrombin time, indicating a prothrombin lowering effect of quinine sulfate. The prolongations varied from 5 to 11.8

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Dr. Harry Neivert made it possible for the authors to conduct this work in his laboratory. Burroughs-Wellcome & Co., Inc., New York, provided the "Stypven" Russell Viper Venom used for the prothrombin estimations.

1. Page, R. C.; de Beer, E. J., and Orr, M. L.: Prothrombin Studies Using Russell Viper Venom: Relation of Clotting Time to Prothrombin Concentration in Human Plasma, J. Lab. & Clin. Med. **27**: 197 (Nov.) 1941.

seconds. On discontinuation of quinine sulfate the raised prothrombin times regressed promptly and approximated the respective control values within a few days.

Subsequently 4 of these subjects were placed on the combined oral medication of 0.33 Gm. of quinine sulfate and 10 mg. of a vitamin K compound daily, and this dosage was continued at least over the period of time in which quinine sulfate alone had produced a significant prolongation of the prothrombin time. The vitamin K compound used in this study was 2-methyl-1,4-naphthohydroquinone-diphosphoric acid ester tetrasodium salt, Synkayvite "Roche." The concurrent administration of vitamin K afforded full protection in all subjects against quinine-induced prothrombinopenia. The dose of vitamin K was an arbitrary one. The minimal amount required to render ineffectual the hypoprothrombinemic action of a given quantity of quinine remains to be determined.

In 2 subjects the combined quinine sulfate-vitamin K medication was followed immediately by a third experimental phase in which again a daily dose of 0.33 Gm. of quinine sulfate alone was given over a period of seven and eight days respectively. Both subjects promptly exhibited another pronounced elevation of the prothrombin time. The accompanying charts portray the experimental procedure, the dosages employed and the results obtained.

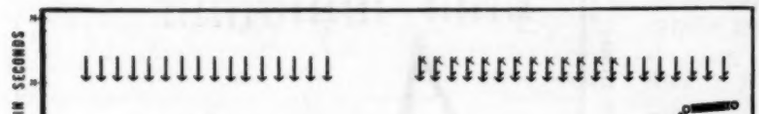

Chart 2.—Representative effects of quinine sulfate on prothrombin time and protective action of vitamin K in M. G., a white man aged 38.

Quinine hydrochloride was employed in two experiments not referred to before instead of quinine sulfate, which was used in the experiments described in this report. The hydrochloride salt also has an unquestionable hypoprothrombinemic action.

The evaluation of the significance of the findings reported awaits further study. While "there are no fixed levels of prothrombinopenia at which bleeding is known to be established" (Shapiro [2]), serious consideration must be given to the thought that prolonged administration of quinine, particularly if larger doses are employed, will interfere with normal blood coagulation. Neivert [3] recently demonstrated that acetylsalicylic acid induced hypoprothrombinemia is one of the most important etiologic factors of late tonsillar hemorrhage. He cautions that where there is wound healing by second intention a hypoprothrombinemic state should be avoided.

According to Sollmann [4] quinine still outranks all other drugs for the routine suppressive and curative treatment of malaria, in view of its effectiveness and low toxicity. Also for mass treatment without adequate medical supervision quinine therapy is most suitable. Strong [5] states that "in certain rural districts the free distribution of quinine has been almost the only important antimalarial measure that it was practicable to conduct."

With the world's most productive cinchona plantations in enemy hands, allied armies fighting in malarious regions are largely dependent on atabrine. For instance, Russell [6] of the Tropic Disease Control Section, Office of the Surgeon General of the U. S. Army, states that "under present conditions quinine prophylaxis is to be used only for men who cannot tolerate atabrine." At any rate the prothrombin blood level of those soldiers, sailors and marines fighting in malaria infested areas who do receive preventive treatment with quinine will be subnormal. If these men are wounded, normal blood coagulability will be impaired, resulting in prolonged bleeding. Later on, oozing from the wounds may occur, particularly if quinine medication is continued. Concurrent vitamin K administration is shown to counteract quinine induced prothrombinopenia. Consequently the combined medication would eliminate the danger of undue bleeding in these subjects.

Also all those malaria patients who, for corrective treatment, receive large doses of quinine for a long time may appropriately be given vitamin K regardless of whether or not there is any likelihood of being wounded. Manson-Bahr,[7] discussing the hemorrhagic forms of malaria, mentions that "hemorrhages may occur in almost any organ." Since quinine because of its prothrombinopenic effect—a property which, preliminary results indicate, is also exhibited by quinidine—is likely to increase the tendency to hemorrhage occasionally present in malaria, the combined administration of quinine and vitamin K will reduce the danger of hemorrhagic manifestations in these patients.

The relation of the present findings to the prothrombinopenic action of the salicylates is of interest. The action of the latter is firmly established [8] and the protective effect of vitamin K against such hypoprothrombinemia has been demonstrated.[9] It is worthy of note that quinine and the salicylates, which have entirely different constitutions, display a certain similarity with regard to their antipyretic action. But this does not

2. Shapiro, S.: Studies on Prothrombin: VI. The Effect of Synthetic Vitamin K on the Prothrombinopenia Induced by Salicylate in Man, J. A. M. A. **125**: 546 (June 24) 1944.

3. Neivert, H.: Lecture given before the Section on Otolaryngology at the New York Academy of Medicine, May 17, 1944, to be published.

4. Sollmann, T.: A Manual of Pharmacology, ed. 6, Philadelphia, W. B. Saunders Company, 1943, p. 599.

5. Strong, R. P.: Stitt's Diagnosis, Prevention and Treatment of Tropical Diseases, ed. 6, Philadelphia, Blakiston Company, 1942, vol. 1, p. 115.

6. Russell, P. F.: Military Malaria Control, War Med. **3**: 565 (June) 1943.

7. Manson-Bahr, P. H.: Manson's Tropical Diseases, ed. 11, Baltimore, Williams & Wilkins Company, 1940, p. 82.

8. Link, K. P.; Overman, R. S.; Sullivan, W. R.; Huebner, C. F., and Scheel, L. D.: Studies on Hemorrhagic Sweet Clover Disease: Hypoprothrombinemia in the Rat Induced by Salicylic Acid, J. Biol. Chem. **147**: 463 (Feb.) 1943. Meyer, O. O., and Howard, B.: Production of Hypoprothrombinemia and Hypocoagulability of Blood with Salicylates, Proc. Soc. Exper. Biol. & Med. **53**: 234 (June) 1943. Shapiro, S.; Redish, M. H., and Campbell, H. A.: Studies on Prothrombin: Prothrombinopenic Effect of Salicylate in Man, ibid. **53**: 251 (June) 1943. Fashena, G. J., and Walker, J. N.: Salicylate Intoxication: Studies on the Effects of Sodium Salicylate on Prothrombin Time and Alkali Reserve, Am. J. Dis. Child. **68**: 369 (Dec.) 1944. Shapiro,[2] Rapoport, Wing and Guest.[9]

9. Rapoport, S.; Wing, M., and Guest, G. M.: Hypoprothrombinemia After Salicylate Administration in Man and Rabbits, Proc. Soc. Exper. Biol. & Med. **53**: 40 (May) 1943.

extend to the antimalarial effect which is peculiar to quinine. The prothrombinopenic action of the two drugs presumably is not related to their main or therapeutically desirable actions, and it is therefore surprising that quinine affects the prothrombin level the same way as do the salicylates.

SUMMARY

Quinine sulfate induces hypoprothrombinemia which can be prevented by concurrent administration of vitamin K. The concurrent administration of vitamin K to combat troops receiving quinine has been suggested for the purpose of eliminating the danger of prolonged, prothrombinopenia-induced bleeding from wounds. The routine administration of vitamin K in conjunction with quinine given for curative treatment is also proposed.

Clinical Notes, Suggestions and New Instruments

NASAL CONGESTION FROM FREQUENT USE OF PRIVINE HYDROCHLORIDE

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Our first clinical experience with privine hydrochloride intranasally in allergic and infectious rhinitis gave us the impression that it was the most effective vasoconstrictor available. The continued use of this drug in our practice, however, began to give us increasing evidence that in addition to its vasoconstrictor action there was a congestive phase. In the last year or so we have been impressed with the large number of patients in whom symptoms of nasal congestion have been aggravated or prolonged by the continued use of privine.

We have seen at least 75 patients, with additional numbers being added every week, whose nasal congestion has been aggravated or maintained by privine. The usual course of events is as follows: The patient having hay fever or perennial allergic rhinitis begins to use privine for relief. Occasionally this start of the continued use of the drug may have its origin in the attempt to relieve the symptoms of a common cold. The medication may have been obtained without order from a physician, usually is prescribed by a physician but refilled without his knowledge, and in some instances was prescribed by us as long as one or two years ago. The patient notices that his nasal congestion is becoming increasingly pronounced, obstruction more complete and lasting and the immediate effect from the drops shorter in duration. Finally the turgescence becomes so severe that he finds it necessary to instil drops every hour or two, even during the night. In the vast majority of instances the privine still continues to show some vasoconstrictor action, so that the sufferer, observing this temporary benefit, does not realize that the same drug is responsible for the increasing congestion of his nasal tissues. Intranasal inspection shows considerable turgescence of the inferior turbinates, giving the typical appearance of vasomotor rhinitis. Smears of the nasal secretion almost always show eosinophils. The exact interpretation of these findings is still open to debate, however, since practically all such cases that we had the opportunity to observe were those of allergic rhinitis in which the condition was aggravated by the use of privine. What the findings would be in persons under similar circumstances is something we hope to be able to report in the future.

In essentially all instances the discontinuance of privine results in much improvement in a week or less. Some patients are reluctant to discontinue what they feel is the only source of relief available. During the first two or three days after the drops are discontinued the nasal obstruction may be severe. During this period it may be advisable to prescribe a sedative to aid sleep; we have used either seconal or pentobarbital sodium. Ephedrine orally may be of some aid, and in occasional cases one may have to allow the sparing use of 1 per cent isotonic solutions of ephedrine sulfate.

Privine hydrochloride is marketed in 0.05 per cent and 0.10 per cent solution, the former being recommended "for children or patients with an extremely sensitive nasal mucosa." Chemically it is 2-naphthyl-methyl-imidazoline hydrochloride, a colorless substance readily soluble in water or saline solution. The marketed solution is isotonic and has a p_H of 6.2, approximating that of the normal nasal secretion. The action of privine, as of other sympathomimetic drugs, is by constriction of the peripheral vascular bed through stimulation of the sympathetic nerve endings. Prolonged action, isotonicity and compatibility with ciliary action are features stressed by the manufacturers. Its vasoconstricting effect is produced rapidly, lasts from two to six hours (in the beginning of its use) and is free of any tingling, burning or smarting.

The congestive effect from continued use of privine might be attributable to one or more possible actions of the drug: 1. It could be assumed that this substance has a vasodilator component in addition to its vasoconstrictor action. 2. The increased vasomotor changes might be due to an allergy to the drug induced by repeated use. 3. The irritability of the tissue could be explained on the basis of chemical irritation or injury if the drug was a primary irritant. 4. The vasodilatation could be due to a simple reaction following an intense and prolonged vasoconstriction.

Epinephrine possesses both a vasoconstrictor and a vasodilator element, referred to as sympathin E and sympathin I, respectively. While the vasodilator effect is weaker, it has a more prolonged action than the vasoconstrictor component. Thus when the vasoconstrictor effect has ceased the dilator factor still operates. Evidence of the presence of these two factors may be found in the so-called "epinephrine reversal," in which ergotoxine or yohimbine is used to paralyze the receptor mechanism in smooth muscle which ordinarily responds to the excitatory action of epinephrine. The administration of epinephrine in yohimbine or ergotoxine treated animals results in immediate vasodilatation without preceding vasoconstriction. For this reason, and probably also because of the dilatation secondary to intense vasoconstriction, epinephrine has been found unsuitable for routine intranasal application. According to Goodman and Gilman,[1] neither ephedrine nor amphetamine (benzedrine) possesses this vasodilator factor. Craver, Chase and Yonkman [2] demonstrated recently that blood pressure reversal was never obtained with privine in yohimbine treated animals. It is interesting to note also that these workers showed that cocaine, unlike its action in combination with epinephrine, does not have any potentiating effect on privine.

It has been inferred by some that the secondary congestive action of privine is due to an allergy induced by the continued local use of the drug. Support for such an explanation of the dilator mechanism lacks good evidence. Other sympathomimetic drugs have shown allergic responses very rarely. Scratch tests with 0.1 per cent privine solution on a number of persons having the typical congestive effect from this drug have been entirely negative. No other manifestations of allergy, such as dermatitis of the skin of the upper lip, asthma or urticaria have ever been noted by us in any users of this drug. It is true that in almost all instances we have found eosinophils in the nasal smear; however, it should be remembered that in our practice we were dealing almost exclusively with patients who were primarily allergic.

Nasal congestion depending on a primary chemical irritation is not a satisfactory explanation of the behavior of privine. This solution is isotonic, has a p_H physiologically compatible with the nasal secretions and is singularly free from smarting, burning or other evidence of primary irritation.

From the Department of Medicine, Division of Allergy, Northwestern University Medical School.

1. Goodman, L., and Gilman, A.: The Pharmacological Basis of Therapeutics, New York, Macmillan Company, 1941.
2. Craver, B. N.; Chase, H. F., and Yonkman, F. F.: Pharmacologic Studies of a New Vasoconstrictor 2-Naphthyl (1') Methyl Imidazoline Hydrochloride (Privine or Naphthazoline): II. Vascular and Respiratory Reactions in the Anesthetized Dog, J. Pharmacol. & Exper. Therap. **82**: 275 (Nov.) 1944.

Vasodilatation as a reaction of intense vasoconstriction is the most plausible mechanism of the action of privine. Increased vasodilatation after constriction is a common phenomenon in exposure to cold, fright and other stimuli. It is to be expected that the degree of such vasodilatation would be dependent on the intensity and duration of the vasoconstrictor action. The relative pressor potency of privine is from one fifth to one third that of epinephrine, while its duration of action is two to three times that of the latter.

A number of other reports have been made dealing with the congestive effect of nasal vasoconstrictors, some of these including or singling out privine. In 1934 Scarano [3] studied the secondary reactions (returgescence, atony and bogginess) following a weekly period of three times daily nasal instillation of ephedrine or amphetamine in oil. Varying degrees of secondary reactions were noted in 5 of 25 cases with ephedrine, while reactions from amphetamine were virtually negligible. During a period of six years Sternberg [4] observed and followed up 32 patients whose nasal discharge and obstruction were more responsible to the continued use of vasoconstrictors than to the underlying allergic condition. A total of eleven different vasoconstrictors was used and the authors observed no evidence as to which one produced most of the damage. Sprays were found to be less harmful than drops. Kully [5] likewise is of the opinion that not one of the sympathomimetic drugs is free from the secondary congestive effect. He states that the degree of congestion is proportionate to the intensity of the vasoconstrictor action and the frequency and duration of its use. He makes the emphatic statement that in many years of observation he has not encountered a single patient who used any of the vasoconstrictors to excess and remained free from the typical after-congestion.

Gollom [6] reported 30 cases in which nasal obstruction was prolonged by the use of privine. The typical histories of his cases are very much like ours, except that apparently in most of his cases the protracted use of the drug followed the attempted relief of a cold. Schiller,[7] in a note to the editor of the *New England Journal of Medicine,* has called attention to the prolonged congestive effect of privine when used in seasonal hay fever. The author states that he has never seen such reactions and addiction following the use of ephedrine or other constrictors. He believes that privine should not be used for a longer time than four or five days.

Even prior to the foregoing reports on privine, in the book one of us [8] published in April 1944 the following statement was made: "We have noted that not infrequently the prolonged use of this drug (privine) establishes a reflex 'rebound,' i. e., an increased congestion after the effect of a single topical application has subsided." This preliminary note, written almost two years ago, has been amplified many times in our subsequent experience. As a matter of fact, the vasomotor rhinitis ensuing from the prolonged use of privine has become one of our most common medical problems in our office practice. The definite amelioration of this troublesome congestion following the discontinuance of the drops has been one of the most dramatic experiences we have witnessed.

SUMMARY

1. Privine hydrochloride, used in nose drops, commonly results in a rebound congestion of the mucosa. This action is due primarily to the vasomotor dilatation as a reaction from the intense vasoconstriction.

2. Other nasal vasoconstrictors may perhaps also produce similar effects, but to a less striking degree. In our practice, however, congestion from the continued use of other constrictors has been noted rarely.

3. The discontinuance of all nasal medication usually results in the alleviation of congestion in a week or less.

4. It is recommended that the use of privine in commonly used concentrations be discouraged in all cases in which prolonged nasal medication is desired. It is possible that further experimentation may indicate that weaker solutions may be better tolerated.

185 North Wabash Avenue.

3. Scarano, J. A.: Rapidity of Shrinkage and Immediate and Secondary Reactions Following Local Applications of Ephedrine and Benzedrine, M. Rec. **140:** 602 (Dec. 5) 1934.
4. Sternberg, L.: The Abuse of Vasoconstrictors in Hay Fever and Vasomotor Rhinitis, New York State J. Med. **44:** 1573 (July 15) 1944.
5. Kully, B. M.: The Use and Abuse of Nasal Vasoconstrictor Medications, J. A. M. A. **127:** 307 (Feb. 10) 1945.
6. Gollom, J.: The Problem of Nasal Medication with Particular Reference to Privine Hcl 0.1%, Canad. M. A. J. **51:** 123 (Aug.) 1944.
7. Schiller, I. W.: Deleterious Effects of Privine Hydrochloride, New England J. Med. **232:** 333 (March 15) 1945.
8. Feinberg, S. M.: Allergy in Practice, Chicago, Year Book Publishers, Inc., 1944, p. 502

THE TREATMENT OF IMPETIGO CONTAGIOSA WITH SULFATHIAZOLE IN AN ALCOHOLIC PLASTIC VEHICLE

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The treatment of impetigo contagiosa has always been an acute problem particularly in children, owing to the extreme contagiousness of the disease. This disease has been reported among war refugees [1] and has recently assumed military importance.[2]

The etiology of impetigo is somewhat obscure and there is no uniform agreement regarding the agent responsible for the disease. Some [3] regard the streptococcus as the etiologic agent, others [4] believe a virus responsible, but the more general opinion [5] is that staphylococci, so prevalent in the lesions, are responsible for the disease. In spite of the fact that reinfection is common among children, one of us (Pijoan) was unable to infect himself with material from impetiginous lesions in various stages of development.

The methods of treating impetigo have been extensive. To the lesions have been applied tinctures of mercurial disinfectants, copper sulfate-zinc,[6] solutions of ferric chloride,[7] boric acid-zinc ointment,[8] staphylococcus toxoid,[9] silver nitrate cautery [10] and the mechanical effect of adhesive plasters.[11] There are also numerous reports dealing with the classic treatment with ammoniated mercury. The successful employment of these chemotherapeutic agents requires the use of surgical dressings. These dressings are difficult to apply especially to such anatomic areas as the ear, nose, mouth and eyelid. They require a great amount of time and often become soiled, moist and loosened.

The use of sulfonamides in the treatment of impetigo has assumed prominence in the last few years. Effective therapy has been accomplished by oral administration [12] and topical application in ointments,[13] powders and microcrystals.[14] More uniform results have been obtained with sulfonamides than with other agents, and these appear to be the drugs of choice for the treatment of impetigo.

Mr. F. V. Worman secured patients for this study.
From the Naval Medical Research Institute, Bethesda, Md.
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Sulfonamides have also been successfully used in the treatment of impetigo,[15] without the use of dressings, by incorporating them in an aqueous plastic vehicle consisting of dimethoxy cellulose or polyvinyl alcohol. These preparations when topically applied dry slowly, leaving a transparent water soluble film through which the lesion may be readily seen. The presence of exudate seems to liberate the drug from the water soluble plastic. While these films are therapeutically effective, the chief disadvantage is their slow drying time from ten to fifteen minutes.[16] The patients, usually children, often become restless and disturb the drying film. This disadvantage has been overcome by the addition of 70 per cent alcohol to the vehicle, which results in a much shorter drying time. While dimethoxy cellulose and polyvinyl alcohol are probably not completely soluble in 70 per cent alcohol, a satisfactory stable dispersion can be obtained by use of the proper technic.

PREPARATION OF SULFATHIAZOLE PLASTIC JELLY

The alcoholic plastic vehicle was prepared by adding dimethoxy cellulose (Dow-Methocel 15 cps.) or polyvinyl alcohol (Du Pont PVA-RH623 low viscosity) to 70 per cent alcohol containing the dissolved sulfathiazole in the proportions given in the following formulas. The preparations are thoroughly mixed in a Waring blendor and allowed to stand for about twelve hours to secure a homogeneous dispersion of the plastic. The methocel mixture is best kept in the refrigerator at + 5 C. during this period, while the polyvinyl alcohol may be slightly heated.

The addition of a small amount of plasticizers to the vehicle is necessary to secure a flexible film which will adhere properly to the skin. Triethanolamine and carbowax and glycerin are used in the formulas given. These preparations have a jelly-like consistency and are best dispensed from a collapsible metal tube.

The addition of 70 per cent alcohol to polyvinyl alcohol (RH-623) or dimethoxy cellulose (cps. 15) shortens the time required for drying as well as to increase the viscosities of these solutions.

The use of 70 per cent ethyl alcohol as a solvent for the preparation of the jellies yields products which are satisfactory in regard to their physical properties. The increase in viscosity results in a more viscous jelly as compared to preparations in which water is used as a solvent. Furthermore, a current of

TABLE 1.—*Comparison of Viscosities and Drying Time of Cellulose and Polyvinyl Alcohol and Water Solutions*

	Ingredients as Gm. or Cc. for Preparation of Jelly			
	Dimethoxy Cellulose		Polyvinyl Alcohol	
0.2 Gm. celluose or 0.4 Gm. PVA used on skin area 6 cm. by 6 cm.	(15 cps.).....10.0 Sulfathiazole..... 1.0 Carbowax (1,500) 3.0 Glycerol..... 1.0		(RH-623).....20.0 Sulfathiazole..... 1.0 Triethanolamine 3.0	
Solvent to a final volume of 100 cc.	70% ethyl alcohol	Water	70% ethyl alcohol	Water
Viscosity (cps.).....	17,378	11,458	4,490	494
Drying time (minutes)..... Wet bulb 60 F. Dry bulb 75 F.	1.5-2.0	4.5-5.0	2.0-3.0	7.0-8.0

air from a fan hastens drying considerably; environmental conditions modify the drying of any substance which depends on evaporation for a result. Excellent adhesiveness is achieved with the plasticizers used, and it is to be supposed that other agents besides sulfathiazole can be incorporated in these jellies. The dry material or film is still water soluble and will dissolve in the presence of exudate and thus liberate a chemotherapeutic agent. When such jellies are spread on skin rather than on lesions they tend to dissolve in sweat, and reapplication may be necessary.

METHOD OF APPLICATION

The impetiginous lesion and surrounding area are soaked with hydrogen peroxide applied with a cotton pledget. Several applications may be necessary to loosen the crusts, which are

TABLE 2.—*Comparison of Therapeutic Results in the Treatment of Impetigo Lesions*

	Location of Lesions					
	Ear	Nose	Circumoral	Scalp	Extremities	Trunk
Number of lesions.....	26	18	20	16	36	15
Sulfathiazole in alcoholic dimethoxy cellulose jelly:						
Number of applications.....	3	1	1	1	1	1
Healing time (days).....	4	3	3	3	2	2
Sulfathiazole in alcoholic PVA jelly:						
Number of applications.....	3	1	1	5	1	1
Healing time (days).....	4	3	3	6	2	2
Ammoniated mercury:						
Number of applications.....	9	6	8	21	5	13
Healing time (days).....	11	6	8	26	7	16
Gentian violet:						
Number of applications.....	13	5	6	20	8	None
Healing time (days).....	19	8	8	24	8	used
Sulfathiazole ointment:						
Number of applications.....	7	13	11	15	5	11
Healing time (days).....	7	8	8	14	7	10

removed by gentle débridement. Rough handling should be avoided, since it will result in increased scar formation. The lesion and surrounding area should be wiped free from excess peroxide and allowed to dry for several minutes. The sulfathiazole jelly is applied in a thin even layer and allowed to dry. One application may be sufficient; however, if further treatment is necessary the jelly may be reapplied without the use of hydrogen peroxide or débridement.

RESULTS

Through the courtesy of F. V. Worman, B.S., M.S.,[17] a bacteriologist collaborating with Dr. E. S. Stong,[17] 54 children with numerous impetiginous lesions were used for study. Approximately the same number of lesions were treated with each of five different preparations.

The therapeutic agents used were the two sulfathiazole plastic jellies, formulas 1 and 2, 3 per cent ammoniated mercury ointment, 3 per cent tincture of gentian violet and 5 per cent sulfathiazole ointment. Bandages were not used with any of the preparations. No difference was noted in the effectiveness of the two sulfathiazole formulas 1 and 2. A comparison of the results obtained with these preparations is shown in table 2.

The therapeutic results obtained by using sulfathiazole plastic jellies varied according to the location of the lesions. The shortest average period required for healing was two days and the longest was six days. The minimum time required to obtain healing with the other therapeutic agents was five days and the longest twenty-six days. In comparing the sulfathiazole jellies with other therapeutic agents without the use of dressings, it should be pointed out that somewhat better results would have been obtained with the other agents had dressings been used.

COMMENT

The topical application of sulfathiazole in an alcoholic plastic vehicle has the distinct advantage of drying rapidly and not requiring a bandage to retain the therapeutic agent in contact with the lesion.

15. Pijoan, M.; Worman, F., and Pijoan, J.: The Treatment of Impetigo Contagiosa with Sulfadiazine-Plastic Preparations and the Exclusion of Dressings, Southwest. Med. **27**: 118, 1943. Worman and Stong.[16]

16. Worman, F. V., and Stong, E. S.: The Treatment of Impetigo Contagiosa by Allantoin-Sulfathiazole in a Polyvinyl Alcohol Vehicle, Rocky Mountain M. J., to be published.

17. Adams State Teachers College, Alamosa, Colo.

The effectiveness of sulfathiazole in plastic jelly in the treatment of impetigo appears to be due to limiting the spread of infection by the plastic film and the bacteriologic effect of sulfathiazole. The presence of exudate liberates the sulfathiazole from the water soluble film at the proper site.

CONCLUSION

Sulfathiazole in an alcoholic plastic jelly is highly effective in the treatment of impetigo contagiosa. The sulfathiazole jelly may be quickly applied, dries rapidly, is soluble in exudate and obviates the necessity for bandaging the lesions.

SUICIDE BY INGESTION OF AMPHETAMINE SULFATE

MAJOR O. L. GERICKE
MEDICAL CORPS, ARMY OF THE UNITED STATES

Death by taking an overdose of amphetamine sulfate is sufficiently rare to warrant reporting such an occurrence. Hertzog, Karlstrom and Bechtel,[1] state that the only fatal case they were able to find reported in the literature was that of Smith[2] in 1939, and they go on to present the case of a 1 year old child who accidentally consumed a minimum of four tablets, or 40 mg., of the drug with fatal outcome.

The comprehensive review of the pharmacology of amphetamine sulfate by Ivy and Krasno[3] cites the case of a student who died a few hours after taking a 10 mg. dose, and the cause of his death remained conjectural in spite of an autopsy.

The present case with death following the deliberate consumption of an estimated 120 mg. of amphetamine sulfate points to the fact that the substance is a therapeutic aid with dangerous potentialities and that the indications for its use should be carefully evaluated before it is prescribed in heroic dosages for narcolepsy, torticollis and other neuropsychiatric conditions.

REPORT OF CASE

A white man aged 36, American, a soldier, was referred for neuropsychiatric consultation by the psychologist during routine screening of absentees because of the unusual finding of his score of 150 on the Wechsler Intelligence Test—in spite of only eight years of schooling and a history of alcoholic spree drinking. The subject related that his childhood was unhappy because his parents were strict devotees of a religious faith which forbade their children modern pleasures, such as attendance at moving pictures, and maintained discipline through the liberal application of corporal punishment. One of the subject's most vivid childhood recollections was of his parents' customary evening journey to religious services, after impressing on the children their firm belief that the end of the world might come in their absence. The children remained fraught with fear during the parents' nocturnal devotions. The patient left this uncongenial home at the earliest opportunity and obtained employment at the age of 16 at a race track in Tijuana, where part of his daily routine for a three month period consisted in the consumption of a quart of whisky. He subsequently did laboring work, served one enlistment in the Regular Army and was a salesman, filling-station operator and fisherman, operating his own boat. In the meantime he married, had a son, was divorced, remarried, and at the time of his interview had also a paramour and an illegitimate child. By now the patient had gained a superficial insight into his personality and recognized the fact that he had periods when he felt "blue" and could gain surcease from his dysphoria by drinking himself into a week-long stupor. Isolation from other people by a solitary fishing expedition was equally efficacious and a much more profitable cure for the "blues." Ultimately, the mutual and sympathetic understanding of his paramour proved able to tide him over his moody spells.

Because of the man's intelligence and interest in his own problem he was given frequent interviews, and therapeutic reading was prescribed, as well as amphetamine sulfate to mitigate his enforced abstinence and avowed feeling of depression. Physical examination was within normal limits, and there was no evidence of psychomotor retardation or depressed facies.

On April 18, 1945 the patient was seen briefly, and he stated that he had had no difficulty in sleeping the previous night, but he complained of loss of appetite. He was given specific directions to take only 5 mg. of amphetamine in the morning and to continue with that dosage until his supply of drug was exhausted.

About 10 p. m. April 18 the soldier attracted the attention of one of his noncommissioned officers and told him he felt ill, whereupon he was transferred to the hospital for admission. A search of his possessions revealed the following letter addressed to the psychiatric social worker, given here as written:[4]

Dear Mr.———,

Ive just made a decision that will seem to you a very weak way of solving this blue-spell, and don't even find reason to really justify it myself but at least you'll not be bothered with having to listen to my crazy explanations that dont even make sense to me.

I've already taken 4 of the pills and Im going to take the rest sometime before morning, I know its going to spoil the Majors experiemtn by taking these pills this way, but they weren't doing any good the other way. I'll be over *this* blue-spell any way I just cant sweat it out any longer, honestly I did try in every way and tried to co-operate with you and the Major in finding the cause, but its no use I just cant think straight even when I try to tell iether of you how I feel and I just feel like a damn fool instead. Thanks any way for all you did, and maybe I did help you in at least understanding a little bit more about the next case you have like mine.

The following running comment was also found and apparently terminated at the time he began to feel so ill that he called for aid:

Its been about 20 min since I took the first 4, dont feel nothing yet but just got through taking 8 more maybe I'll get that elated feeling one more time at least, if a dozen dont do it Ill keep taking them 4 at a time till they do. If I live through this, I'll at least know how it feels to come from the depths to the hieghts. its made me belch twice that all, well of all the places to feel a sensation my right foot feels like its getting numb. my heart is pounding and I feel a pulse in my head that seems to start from behind and go around counter clock-wise and stop about even with my left ear. I sure as hell dont feel any elation though only a determination to carry this through and stop these blues once and for all. If they know very little about them with all their knowledge how the hell can I ever know whats causing it. Its funny but I dont feel sorry for myself or that Im a martyr about this. I always figured that people who took this way out were weak and yet I dont feel that way about myself, must be ego I guess. Ive no new feelings so Im going to take 4 more. my temples are pounding now and it feels like my legs were away off

The soldier was admitted at 10:15 p. m. and the admitting officer noted that he was in a dazed condition. His pulse rate was 58, strong and full. The pupils reacted to light and in accommodation and he complained of an intense headache, frontal in type. A mannerism of continually sweeping the left hand over the forehead and left eye was present. The nurse's notes give the additional information that the patient appeared wide awake on entry but seemed very nervous. At 11:30 the nurse noted that the patient's right leg and arm were paralyzed; he had difficulty with breathing and was involuntary. At 12:30 a. m. the pulse rate was 56; respiration was not labored, and the blood pressure was 140/80. Questions were answered with difficulty. The right leg and arm appeared paralyzed; however, reflexes were present. His condition remained the same, the pulse becoming somewhat stronger, and at 2:30 the pulse rate was 80, the color was good and respiration was not labored. His condition remained stationary until 4 o'clock, when an attack of vomiting occurred. The vomitus consisted of a brownish fluid. At 4:05 the rectal temperature was 103.8 F. Caffeine and sodium benzoate and administration of oxygen failed to bring about any improvement in his condition. The respirations were labored, the pulse was over 100 and the patient's condition became steadily worse until he died, at 4:55 a. m. on April 19.

Autopsy showed no gross findings of interest until the cranial vault was removed and the dura exposed, when the autopsy surgeon noted that the cerebral hemispheres showed a flattening of the convolutions, and there was a dark hemorrhagic

1. Hertzog, A. J.; Karlstrom, A. E., and Bechtel, M. J.: Accidental Amphetamine Sulfate Poisoning, J. A. M. A. **121**: 256 (Jan. 23) 1943.
2. Smith, L. C.: Collapse with Death Following Use of Amphetamine Sulfate, J. A. M. A. **113**: 1022 (Sept. 9) 1939.
3. Ivy, A. C., and Krasno, L. R.: Amphetamine (Benzedrine) Sulfate: A Review of Its Pharmacology, War Med. **1**: 15 (Jan.) 1941.

4. Such errors in grammar and spelling as are found in the letter had not appeared in the previous writing of the patient. Their appearance here may be ascribed to his physiologic state.

area approximately 4 cm. wide extending from the right temporal lobe upward and backward along the central fissure to the longitudinal fissure. A small cut section through this area revealed the hemorrhage to be about 1 cm. in depth, and it extended above the arachnoid space into the brain tissue. There was a blood clot approximately the size of a walnut in the cerebellopontine angle. The entire brain was removed for further section. The brain tissue was so extremely soft and friable that it could not be preserved intact.

The pathologist, on examination of tissue submitted to him, noted a mass of clotted blood measuring 7 by 4.5 by 2.5 cm. beneath the dura on the right side. Over the right cerebral hemisphere there was considerable subarachnoid hemorrhage involving the parietal and anterior portion of the occipital lobes. There were no areas of contusion involving the brain substance. Considerable congestion throughout the white matter of the cerebral hemispheres was observed, and several tiny petechiae were present. There were multiple small hemorrhages of the pons. The cerebellum showed a few tiny "ring" hemorrhages. The final diagnosis was:

Cardiovascular: Coronary arteriosclerosis.

Respiratory: Pulmonary congestion and edema. Pulmonary emphysema.

Spleen: Congestion of spleen.

Genitourinary: Congestion and hemorrhages of kidney.

General nervous system: Subdural and subarachnoid hemorrhage, right parietal and occipital lobes. Petechial hemorrhages of cerebrum and cerebellum. Hemorrhage of pons.

An analysis of the stomach contents was negative for amphetamine sulfate.

SUMMARY

Death of a 36 year old man followed the ingestion of an estimated 120 mg. of amphetamine sulfate taken with suicidal intent. The immediate cause of death was subdural and subarachnoid hemorrhage of the parietal and occipital lobes.

Council on Industrial Health

MASS HEALTH SURVEYS IN INDUSTRY

This statement has been prepared by the Council on Industrial Health and approved for publication.

C. M. PETERSON, M.D., *Secretary.*

An important component of industrial health examinations is the discovery of nonoccupational disease, often in incipient and readily manageable stages. Early detection of illness and prompt adequate treatment are in the best interests of the worker, the employer, the community and the medical profession.

Increasingly in recent years official and voluntary health agencies have regarded industry as a convenient avenue for special case-finding campaigns—especially tuberculosis, syphilis and defective vision. All have important relations to the general public health or are designed to improve production and earning power or to reduce troublesome absenteeism and wastage.

The Council on Industrial Health believes that these case-finding campaigns conducted in industry by outside agencies merit support and cooperation from the medical profession provided certain general principles are observed:

1. The local medical profession, health authorities and other affected community health facilities should be fully advised well in advance about the purposes and scope of the survey.

2. The personnel undertaking the survey must be professionally competent and employ acceptable equipment and procedure. Results of examinations should be interpreted by physicians of experience and training in the methods employed.

3. Mass health surveys are essentially screening operations. Unless preliminary agreement suggests otherwise, the details of confirmatory diagnosis should be regarded as responsibilities of the established medical, clinic or laboratory facilities in the community.

4. Full consideration needs to be given to the disposition of individuals with clinically significant findings. They should be promptly referred to personal physicians or other authorized community agency for additional study and individualized treatment.

5. Means for isolation, hospitalization or other essential treatment need careful evaluation in advance of the survey.

6. Reporting and epidemiologic investigation of communicable disease should conform with the regulations of the health department having jurisdiction.

7. Surveys should be conducted only after the plant medical service has had an opportunity to study the proposed activity and given its approval. The details of case finding should conform to accepted industrial health procedure and be integrated with the regular activities of the plant medical department. The industrial physician should be consulted particularly (*a*) on discovery of coincidental disease or disability having suspected occupational etiology, (*b*) regarding plans for referral of patients and follow-up and (*c*) about the details of reemployment, especially placement in suitable occupations of individuals with residual impairment.

Council on Pharmacy and Chemistry

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

AUSTIN SMITH, M.D., *Secretary.*

HEXAVITAMIN TABLETS.—"Hexavitamin Tablets contain in each tablet not less than 2,500 U. S. P. units of vitamin A from natural (animal) sources, 200 U. S. P. units of vitamin D from natural (animal) sources, or as activated ergosterol or activated 7-dehydrocholesterol 37 mg. of ascorbic acid, 1 mg. of thiamine hydrochloride, 1.5 mg. of riboflavin and 10 mg. of nicotinamide."—U. S. P.

For description and standards see the U. S. Pharmacopeia XII First Bound Supplement under Tabellae Hexavitaminarum.

Actions, Uses and Dosage.—For prophylaxis and treatment of conditions arising from deficiency of vitamins A and D and ascorbic acid, thiamine, riboflavin and nicotinic acid. See articles on the various vitamins concerned (N. N. R. 1944, pp. 604-625).

INTERNATIONAL VITAMIN CORPORATION, NEW YORK

Tablets Hexavitamin: Each tablet contains 2,500 U. S. P. units of vitamin A, 200 U. S. P. units of vitamin D, 37 mg. of ascorbic acid, 1 mg. of thiamine hydrochloride, 1.5 mg. of riboflavin and 10 mg. of niacin amide.

NICOTINAMIDE (See New and Nonofficial Remedies 1944, p. 617).

The following additional dosage form has been accepted:

GEORGE A. BREON & CO., INC., KANSAS CITY, MO.

Tablets Nicotinamide: 100 mg.

TRIASYN B.—"Triasyn B Capsules and Tablets contain in each capsule or tablet not less than 1 mg. of thiamine hydrochloride, 1.5 mg. of riboflavin and 10 mg. of nicotinamide."—U. S. P.

For description and standards see U. S. Pharmacopeia XII First Bound Supplement under Capsulae Triasyni B and Tabellae Triasyni B.

Actions, Uses and Dosage.—For prophylaxis and treatment of conditions arising from deficiency of thiamine, riboflavin and nicotinic acid. See articles on the various vitamins concerned (N. N. R. 1944, pp. 606-615).

PREMO PHARMACEUTICAL LABORATORIES, INC., NEW YORK

Tablets Triasyn B: Each tablet contains 1 mg. of thiamine hydrochloride, 1.5 mg. of riboflavin and 10 mg. of nicotinic acid amide.

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SATURDAY, AUGUST 11, 1945

FEDERAL PROGRAMS TO PROMOTE SCIENTIFIC RESEARCH

Under the Organization Section in this issue of The Journal appears an analysis of legislation pending in the 79th Congress to implement the recommendations regarding research contained in the report recently submitted to President Truman by Dr. Vannevar Bush. In addition to the proposals analyzed in this article, several others have been introduced with a view to continuance in the postwar period of the coordinated and intensified research that did so much for the advancement of medical and other sciences during the war. For instance, one measure introduced by Mr. Thomas of Utah on July 26 is designed toward increasing interest in children while they are in secondary schools.

The number and diversity of the measures proposed are themselves an evidence of the difficulty of finding a formula for the purpose that will accomplish the desirable objectives without introducing factors harmful both to research and to our system of government. Surely every one concerned would wish to avoid bureaucratic domination of research, inhibition of investigations carried on under private initiative, in industry, in schools and colleges or even by individuals, and the spending of funds without any reasonable likelihood of adequate return. Practically all the measures propose to develop a national research foundation as an independent agency in the executive branch of the government, yet there is no obvious consensus as to the way in which such an agency should be established, the funds that should be granted to it, the technic of its operation, the choice of its personnel, the duration of its activities or the manner in which it would cooperate with existing governmental and private organizations. Senator Kilgore himself recognized these difficulties in his hope that joint hearings might be held so that the issues presented by these bills could be clarified.

While these measures propose to coordinate and intensify research in various scientific fields, they would seem to demand a certain amount of coordination within their own proposals. Among the objectives sought are the stimulation of research in physical sciences, medicine and the national defense. Obviously advancement of medical science is a contribution to the national defense, as are no doubt also advances in the physical sciences. Nevertheless discoveries related to bombing, chemical warfare, new weapons and new technics of defense, aviation and transportation are somewhat remote from the control of infectious diseases, the detection of viruses and the prevention and cure of epidemic diseases. Discoveries in physics, chemistry and related sciences are often promptly explored for such benefits as they will yield in the diagnosis, prevention and treatment of disease, yet these are quite certainly not as closely related to medicine as are anatomy, physiology, pathology, bacteriology and immunology. The advancement of research in the medical sciences is indissolubly associated with undergraduate and graduate medical education, the functions of the hospitals and the practice of medicine. Some of the proposals completely ignore these necessary relationships.

Most of the proposals request a managing board of limited numbers with subsidiary advisory boards in the fields that have been mentioned. Without specific allocation of funds or influence to these subsidiary fields, the pressure of public opinion rather than the immediate good to the public may be the determining factors in the allocation of such funds as are made available. One of the dangers inherent in federal assistance is the possibility of a type of federal control over research and the results of research that would prevent the dissemination of new information and inhibit rather than stimulate investigative activities. Moreover, bureaucratic direction may serve to monopolize personnel to the extent of depriving private industry, private educational and research institutions and other nongovernmental agencies of the opportunity to secure workers in a field in which the number of competent investigators is always less than the demand for them.

Already agitation is obvious in behalf of the social sciences, sociology, psychology, economics and similar fields of learning. Surely such sciences might also benefit by the type of aid that government can render, yet the possibilities even with the physical sciences and with medical science have not been explored. The establishment of a pattern for action by the government in stimulating science might well be developed by the experimental technics of science before application is made to every phase of human life and learning.

The considerations that are here merely suggested are only a few of hundreds of questions that have already arisen in the minds of all those concerned with these projects. The least that Congress could do, under the circumstances, would be to provide for extensive hearings under proper conditions with representation from many interests before a measure that would include what seemed to be the most desirable features of all the proposals could be compiled. Even this measure when finally developed should be again submitted to new hearings before definite action by the Congress would seem to be warranted. Such delay as would be required might seem unfortunate, particularly now when all the world recognizes the accomplishments of science during the war and when every one would wish to retain in the postwar world the advantages that have been gained by coordinated and intensified research. Nevertheless the harmful potentialities in these projects are sufficiently apparent to require at least enough time for careful consideration before definite action is taken.

THE MATERNAL AND CHILD WELFARE ACT OF 1945

Senator Pepper and nine other members of the Senate Committee on Education and Labor have introduced a bill (see Organization Section, page 1112, this issue) designed to extend the provisions of the Social Security Act by increasing materially the funds available for maternal and child health services, services for crippled children, child welfare services, and an increased personnel of the Children's Bureau necessary for administration. Included are suggestions for research and for education of personnel. This bill is perhaps the official opening of a campaign to make permanent some of the activities that prevail under the so-called EMIC program.

Early in the establishment of EMIC, THE JOURNAL predicted that the Children's Bureau would not be happy until permanence had been given to this tremendous expansion of its activities. As with much other legislation for social welfare, few would oppose the objectives sought, namely promotion of the physical and mental health of mothers during maternity and of their children, preventive health work and diagnostic services for children, school health services, the care of sick children and the correction of physical defects. The allotment of federal funds to the individual states is now a well established principle in our government. The public has a right to ask that need be established before funds are allocated. The wisdom of placing control in the Children's Bureau through insistence that plans must be approved by the chief of that bureau before funds can be granted is subject to doubt. The chief of the Children's Bureau is to formulate the policies after consultation with the state health officers and an advisory committee. Nothing in the act says that the advisory committee is to have any authority or that its advice need necessarily be followed. THE JOURNAL has previously criticized adversely the political technic which permits the chief of a government bureau to select his own advisory committee and then even to disregard the advice of the committee that he himself selects.

In submitting the bill, Senator Pepper offered some interesting estimates. Thus he said:

> Medical care and health supervision of children is costly in dollars. Reliable authorities estimate it comes to somewhere in the range of $25 to $40 a year for each child in the United States. With 40,000,000 children under 18 that represents a total of at least $1,000,000,000 for the country. A federal appropriation of $75,000,000 for maternal and child health and for crippled children for a year cannot go very far in meeting these all-over health needs of children.

Almost coincidentally with the offering of this proposal came an announcement in the press indicating that Secretary Schwellenbach of the Department of Labor desired to see the Children's Bureau removed from that department and possibly incorporated in a new department of the government to be devoted to health and welfare. Whether or not President Truman, in his apparent wish to consolidate government agencies, will suggest the establishment of a new department in the cabinet to include the Children's Bureau, that agency long since should have been integrated with the other health activities of the nation.

ARMY ROUTINE IN TREATMENT OF MALARIAL ATTACKS

Discharged soldiers who have had malaria may have clinical attacks many months after leaving the service. Most of these attacks will be due to vivax infections. Of 18,171 analyzed attacks occurring in the United States in soldiers infected while oversea, 98 per cent were due to Plasmodium vivax alone. The attacks are generally mild and respond quickly to adequate treatment. Among 32,292 admissions for malaria to army hospitals in the United States in 1944 two deaths were attributed to the disease.

Febrile illnesses in discharged soldiers who have served in malarious regions should raise the suspicion of malaria. Thick blood films should be examined for parasites in such cases. The possibility of malarial relapses in ex-soldiers who undergo surgical operations must be kept constantly in mind. While it may occasionally be necessary to treat patients without an accurate laboratory diagnosis, such practice is dangerous and should not become routine. Other diseases for

which specific therapy is essential, such as pneumonia or meningitis, may be overlooked, with tragic results.

In general, the Medical Department of the Army on the basis of a huge experience prefers to use atabrine in treating usual cases of malaria. The standard Army treatment consists of 1 Gm. in divided doses in the first twenty-four hours, followed by 0.1 Gm. three times a day for six days.

As an alternative to atabrine for patients who do not tolerate atabrine, quinine, when available for oral use, or totaquine, which is freely available, may be used. The dosage of both of these drugs, as used in the Army, consists of 1 Gm. three times a day for two days, followed by 0.6 Gm. for five days. In civilian practice it is believed that this dosage could with safety be reduced slightly, especially for relapses of vivax malaria. Clinical studies by the Army both in the United States and overseas show that, in the dosage given, totaquine U. S. P. gives results as satisfactory as those secured with quinine.[1]

Many helpful details with regard to diagnosis and treatment, including the management of complicated and severe cases requiring parenteral treatment, are given in a recently published War Department Technical Bulletin.[2]

Available treatment will not prevent relapses of vivax malaria. Investigations by the Medical Department have shown clearly that courses of treatment like those given for clinical attacks are useless between relapses. To avoid the occurrence of attacks in close succession the Medical Department recommends that treatment for attacks be continued with small doses of an antimalarial for a variable period, usually at least ninety days. Atabrine is usually employed. The continuation dosage, which should not be exceeded, is 0.1 Gm. a day. On this dosage relapses rarely occur. If quinine is used, the Army found 0.6 Gm. a day necessary in oversea practice. This is a troublesome amount of quinine to take continuously, but breakthroughs were fairly common overseas when smaller doses were taken. Further information on this aspect of the subject is provided in another Technical Bulletin, Med. 136, on the Avoidance of Relapses of Vivax Malaria by Use of Suppressive Medication.

Physicians should exercise care in the choice of an antimalarial drug. Individuals who are sensitive to atabrine or seriously intolerant of it should receive totaquine or, if available, quinine. Similarly, persons who are sensitive to totaquine or quinine should receive atabrine. It should be remembered that totaquine U. S. P. contains about 10 per cent quinine. Persons sensitive to both atabrine and the cinchona alkaloids are seen only rarely.

1. Bull. U. S. Army M. Dept. number 84, January 1945, p. 51, number 89, June 1945, p. 21.
2. Treatment of Clinical Malaria and Malarial Parasitemia, Tech. Bull. Med. 72, War Dept.

Current Comment

DISCHARGE OF MEDICAL OFFICERS

In this issue of THE JOURNAL appears the official statement of the Army Medical Department relative to the discharge of medical officers. The Connecticut State Medical Society late in July adopted a resolution which was sent to the Board of Trustees of the American Medical Association and presumably to the officers of other state medical societies, urging that the American Medical Association "press the reactivation of the Procurement and Assignment Service in a workable and liberal advisory authority concerning the separation of medical officers and restore to it the same responsibility it exercised during the period of recruitment of medical officers." The resolution urged further that the American Medical Association and its components should seek the interest of the Congress of the United States in providing a clear and productive separation policy for medical officers. . . ." The policy presented in this issue of THE JOURNAL is one on which the officials of the United States Army and of the Army Medical Department have been working for some time. Recently the Michigan State Medical Society took action similar to that of the Connecticut State Medical Society. The organization known as the Association of American Physicians and Surgeons, Inc., according to the press, has sent a resolution to numerous officials of the government. This resolution lists a number of rumors, most of which are without the slightest foundation in fact. The officials of the Association of American Physicians and Surgeons could have found out how completely unwarranted these statements were before giving them publication and thus promoting dissatisfaction and disintegration of morale without the accomplishment of any conceivable worthwhile objective. Meanwhile word comes from Washington that the War Department has assigned Col. William P. Holbrook to help the Military Affairs Committee of the Senate investigate charges of overstaffing of doctors in the Army. Colonel Holbrook is to assemble all pertinent statistics on medical personnel and to have them ready for the committee when Congress reconvenes on October 8.

HEALTH LEAGUE OF CANADA

A report of the twenty-fifth annual meeting of the Health League of Canada, with headquarters at Montreal, is sent out in anticipation of the league's twenty-sixth annual meeting, scheduled for September 1945.[1] The silver anniversary publication reflects public health progress in Canada. The league has five technical divisions, dealing with immunization, industrial health, venereal disease, nutrition and pasteurization of milk. These are considered the five major challenges to health in Canada. Under these various headings important

1. Report of the Twenty-Fifth Annual Meeting of the Health League of Canada at Montreal, Nov. 23-24, 1944.

needs are stressed, such as medical examination before marriage and antepartum examinations. These objectives are being attacked by the usual methods in health education: pamphlets, films, posters and local meetings and letters. Under the heading of Immunization, the educational attack was on diphtheria, smallpox, whooping cough and, in some provinces, scarlet fever; 20,000 lines of sponsored advertising in forty Canadian newspapers featured this campaign. The industrial health division has functioned mainly through the distribution to industry of posters, pay envelop inserts and instructive booklets; conferences also have been held. Production of a nutrition calendar was a prominent activity. Little progress is reported toward pasteurization of milk; only the province of Ontario requires the pasteurization of all milk. The Health League of Canada represents in Canada many of the activities which are carried on in the United States by special independent agencies known as voluntary health agencies. In view of current agitation of the issue of consolidation or federation of voluntary health agencies in the United States, the functioning of the Health League of Canada for a quarter of a century should offer interesting examples. While nations differ, there are probably no two peoples more alike than those of Canada and the United States. The Health League of Canada has an official publication, *Health*, which is published quarterly and reaches a coast to coast audience "of well over thirteen thousand readers."

RADIO TRANSCRIPTIONS FOR HEALTH GROUPS

On page 1114 of this issue of THE JOURNAL the Bureau of Health Education announces the seventh series of electrically transcribed radio broadcasts for local use by medical societies or by local health or welfare groups with the approval of the local medical society. With the addition of these transcriptions, this important and growing service now represents a well rounded coverage of the field in health education. A series titled Medicine Serves America deals with medical progress. Live and Like It, a dramatized series, considers the everyday health problems, such as weight control, sleep, prompt medical care and superstitions. Before the Doctor Comes is a series of informal question and answer discussions with doctors about common symptoms occurring in the family, such as cough, rash, earache, bleeding and similar minor but perplexing problems which must be faced while doctors are scarce. There is a series of twelve programs called Dodging Contagious Diseases: this title is self explanatory. For local societies desiring to remain on the air through the summer, twelve transcriptions are available under the title Keep Cool, which deal with summer problems such as suntan, swimming, bugs, poison ivy and hay fever. Health problems of middle age are dealt with in a series of thirteen platters featuring interviews with thirty-three prominent public health experts. The health problems of middle age form the subject of the series More Life for You, in which twenty-four medical and surgical authorities are interviewed. These seven series, a total of eighty-eight broadcasts, will suffice to keep a medical society or other local group on the air weekly without interruption for almost two years. The diversification of subjects allows for scheduling with regard to seasonal timeliness. The diversity of approach, including interviews, round table and dramatization, will lend variety and interest to the local series. Further information may be had by addressing the Bureau of Health Education, 535 North Dearborn Street, Chicago 10.

NARCOTIC PRESCRIBING BY TELEPHONE

The United States Commissioner of Narcotics has called attention to the difficulty that has resulted throughout the country because of the frequency with which physicians telephone their narcotic prescriptions. This practice, he reports, has resulted in abuse and in illicit traffic, many pedlers and addicts using this means to obtain morphine. In at least one community the practice has resulted in a federal grand jury investigation. The report of this grand jury, after describing the facts developed during the investigation as disclosing "a rather shocking disregard of the law" and as reflecting a condition "intolerable and wholly unwarranted," continued:

> We do not wish to place ourselves in a position or attempt to determine when or under what manner or in what quantities a person may need narcotics for the alleviation of pain or suffering, but we feel that we are in position to say that the conditions above referred to are intolerable and wholly unwarranted and, if continued, can only result in an indictment wherever warranted. It has been stated in defense of this condition that the doctors are overworked and prescriptions by telephone are time savers. We are conscious of the overworked condition of most of our physicians, but we disagree with the contention that such practice is warranted in order to save time. It is a matter of obeying or violating the law.
>
> We are making this report at this time in the hope that these abuses, as well as any others not mentioned herein, may be speedily corrected. We propose to pursue this investigation further when next called and will then take such action as the facts and circumstances warrant at that time.

Under existing regulation, the furnishing of narcotics pursuant to telephone advice of physicians is prohibited, whether prescriptions covering such orders are subsequently received or not, except in an emergency. In such an emergency, a druggist may deliver narcotics through his employee or responsible agent pursuant to a telephone order only if the employee or agent is supplied with a properly prepared prescription before delivery is made and this prescription must be turned over to the druggist and filed by him as required by law. Physicians will aid materially in preventing the abuse referred to by the Commissioner of Narcotics if they restrict orders for narcotics by telephone strictly to actual emergency cases.

MEDICINE AND THE WAR

REDEPLOYMENT AND SEPARATION OF MEDICAL DEPARTMENT OFFICERS

NOTE.—*Following is the text of the official announcement released by the Office of the Surgeon General, U. S. Army, relative to the discharge of Medical Officers.*—ED.

V-E Day found the War Department with approximately 65 per cent of its Medical Corps officers overseas, the largest number in the European and Mediterranean theaters, the others principally in the Pacific. Some time prior to the announcement of V-E Day the War Department had completed its planning for redeployment, readjustment and discharge. This plan provided for discharges of enlisted personnel in relation to the declining requirements of a one front war, based on length of service, length of overseas service, combat activity, decorations and number of dependents. The composite score was known as the Adjusted Service Rating. The separation of officers was not tied down initially to a specific Adjusted Service Rating although the War Department desired that, within the limits of military necessity, substantially the same type of equitable, objective considerations should govern.

The War Department's pre-V-E Day planning also laid down the principles to govern the movement of personnel out of the European and Mediterranean theaters once victory was achieved. Military necessity, governed by consideration of transportation and the strategic requirements of the Pacific, scheduled the movement of a considerable number of troops directly from Europe to the Pacific. This was particularly true of service troops—the Engineers, Signal and, to a lesser degree, Medical Personnel—which were to prepare the way for the large inflow of divisions which would arrive in the Pacific after a short period of furlough and retraining in the United States.

Within the limits of military necessity, which govern here as in every other phase of redeployment and discharge policy, men with the lowest Adjusted Service Ratings were to go to the Pacific directly. Those with a large number of points were to go to the Pacific via the United States or were to remain in the United States as a strategic reserve until a final decision could be reached concerning the need for them during the remainder of the Japanese war. Men with a still larger number of points would remain in Europe as the Army of Occupation, while those with the highest points would be returned to the United States as surplus. It did not follow that the surplus group would necessarily be discharged, since it was possible—in fact, probable—that some of these men might have lower scores and therefore be less entitled to discharge than others who had returned from overseas at an earlier date or were now in the Pacific awaiting replacement before they could be returned. To permit the discharge of men with low scores because the war in Europe was over and they could be brought home, while men with substantially higher scores would be forced to continue fighting in the Pacific, was clearly inequitable. A responsible policy had to provide for sending replacements to the Pacific to permit the return of their high score personnel for discharge.

While V-E Day found the Medical Department with approximately 35 per cent of its Medical Corps strength in the United States, the same did not hold for other arms and services. All of the divisions were out of the country, and the same was true of the Signal Corps, Engineer and other service personnel. The Medical Department had considerably more of its personnel in the United States because of the fact that the definitive care which the battle wounded received is given them, not in overseas hospitals, but in the large general and convalescent hospitals in this country. Likewise there remain many hospitals in the United States which provided medical care for the Service and Air Force troops still in this country as well as for the inductees and trainees. These hospitals had to be manned, and it had not been feasible nor desirable during the relatively short European war to exchange personnel between the United States and Europe. Extreme exigencies in shipping had placed great difficulties on exchange with the Pacific.

In working out the over-all plans for redeployment, it was logical to envisage that most personnel adjustments would be made in Europe, with the divisions cleared for the Pacific on embarkation, permitting the pesonnel a thirty day leave in the United States and providing for them a short retraining period to prepare them for the differences in Pacific warfare. There was no room in this plan for adjusting personnel once the divisions returned to the United States, since there was no one left here for exchange purposes, except a few raw recruits.

The Medical Department picture was, however, markedly different. Cognizant of these differences the Surgeon General requested and received permission to exchange personnel in the units coming through the United States to the Pacific on the condition that the units would be able to perform their mission at the time they left this country.

Over-all planning of the Surgeon General went beyond this one step of restaffing units in the United States.

During the spring of 1945, when the European war was reaching its climax and the Pacific war was accelerating, the Surgeon General had stripped the United States of all personnel that could possibly be spared to provide the fighting fronts with the maximum number of medical personnel. However, as the war in Europe began to draw to a close every effort was made to bring back the battle wounded as rapidly as possible, so as to avoid the errors of World War I, when the wounded were forced to wait for many months because of shipping stringencies. Not only was care taken to avoid a repetition of this, but it was essential that many European and Mediterranean hospitals be cleared quickly so that they could meet the early dates set for direct movement to the Pacific. Early 1945 found the European Theater with more than 191,000 patients; by the end of June this figure was approximately 65,000. May and June saw the return to the United States of 98,000 patients, all but 24,000 of whom came from the European and Mediterranean theaters.

During the first half of 1945, when the maximum numbers of medical personnel were being sent overseas, the number of patients remaining in the general hospital system in the United States, which treats almost exclusively overseas casualties, increased from 133,000 to 240,000.

With personnel flowing out and patients flowing in, the Surgeon General had planned long before V-E Day to request the return of Medical Corps officers as soon as the fighting in Europe ceased. A substantial requisition was placed on the European theaters shortly after V-E Day, but the tremendous

personnel shift in the theater and the uncertainty regarding individual scores, which were not available until almost six weeks after V-E Day, made it difficult for the theater to return personnel as rapidly as desired. Such personnel has by this time returned or is en route.

Permission to restaff the units coming through the United States and the early return of personnel to assist in the operation of the hospitals in the United States constitute but two of the four phases of the Surgeon General's plan. Realizing that the units which had to go from the European and Mediterranean theaters directly to the Pacific had to be filled not only in number but also with the proper types of specialists so that they could perform their mission on arrival, and realizing further that the Mediterranean in particular would have to dip down into personnel which had two or more years' overseas service to find specialists to balance these units, the Surgeon General recommended exchanges between the European and Mediterranean theaters to avoid sending high score personnel to the Pacific. After some delays this policy was put into effect, but it will not completely obviate the unfortunate situation in which certain scarce specialists will have to proceed directly to the Pacific without passing through the United States because the exigencies of war permitted no delay in shipping dates.

The final point in the Surgeon General's plan was to prepare the groundwork for an accelerated exchange of personnel with the Pacific, as soon as part of the surplus personnel in the European and Mediterranean theaters was returned to the United States, so that replacements could be sent from the United States to the Pacific.

To implement the restaffing of units scheduled for the Pacific coming through the United States, a complete census was undertaken of all personnel stationed in the United States. On the basis of this census and in light of experience to date, criteria were established for withdrawing personnel from units passing through the United States and for assigning personnel now in the United States to the units scheduled for the Pacific.

These are only general rules and are subject to exception in any case due to military necessity, and to change if subsequent developments should make such action necessary. They are not to be understood as creating any right in an officer to continue on duty in this country if military needs now or later should require his assignment to other duty. Subject to these qualifications, the plan for withdrawal of officers from units and for new assignments is shown in the accompanying table.

The fact that more stringent criteria for withdrawal and assignment were established for Medical Corps officers than for other Medical Department Corps reflected smaller availabilities of Medical Corps officers than of other Medical Department Corps.

Because there is nothing in this plan of medical redeployment which takes precedence over considerations of military necessity, it will not be possible to apply the withdrawal principle to Commanding Officers and Executive Officers of hospital units or to certain Medical Department personnel attached to divisions because adequate replacements cannot be found and trained within the available time.

Moreover, there is nothing in the plan which stands in the way of volunteering. If an individual desires service in the Pacific, he can go if he passes the physical qualifications, irrespective of age, score or prior overseas experience.

Despite the above qualifications, it is hoped that the criteria outlined in the preceding table can be followed in the case of the vast majority of Medical Department officers returning through the United States for redeployment to the Pacific.

Intimately associated with the problem of redeployment are problems of readjustment and discharge. Reference has already been made to the fact that the original plan of the Surgeon General contemplated the sending of replacements to the Pacific at the earliest possible date, in order to permit the return to the United States of personnel who have had long overseas service. One phase of this plan is already in operation. Large numbers of nurses who have been in the tropics for two or more years will soon have the opportunity of returning to the United States while the theater will have the benefit of a group that has not yet suffered from the exhaustions incident to life in the tropics and to combat.

At first glance it might appear difficult to understand how it happens that several months after V-E Day, with the scale of combat having shrunk from a two to a one front war, the Army has only now begun to separate Medical Corps officers and other Medical Department personnel. The 98,000 patients who were brought back to the United States in May and in June were preceded in March and April by 89,000 patients, or a total of 187,000 patients during a four month period. On the basis of detailed experience tables for World War II, the average overseas casualty returned to the United States for definitive treatment remains in a hospital in this country for five to six months. This means that, although there have been only Pacific casualties since V-E Day, there were a sufficient number of casualties prior to V-E Day to keep the general and convalescent hospitals in this country operating at or near peak until late fall of this year. The Medical Department personnel that are attached to divisions in Europe and in the Mediterranean have, of course, not been busy with the care of casualties since V-E Day, although a considerable number were forced to assume the job of caring for the thousands of sick and wounded displaced persons in the areas overrun by the American armies. However, this "divisional" personnel has for the most part been busy dismantling forward hospitals and moving to the staging areas for embarkation either directly to the Pacific or through the United States. In addition, there are many thousands of Medical Department officers at the present moment on the high seas and many other thousands on leave in the United States preparatory to taking up assignments in this country, so that others who have not yet been overseas can go.

When hostilities ceased in Europe, the worldwide medical picture was this: an expanded war in the Pacific with vastly increased requirements, not only to cope with the engagements that were to be launched, but to facilitate the return to the United States of large numbers of personnel who have had long service in the Pacific for reassignment or separation. The United States had a peak patient load and would soon have thrust upon it a substantially increased medical processing load incident to the return of troops for redeployment to the Pacific or for discharge. This meant that the surplus brought about by a shrinkage from a two to a one front war was largely in Europe, where it could not be used for any of the strategic purposes for which it was needed: that is, to permit the separation of high score personnel, which could only take place

Plan for Withdrawal and Assignment of Officers

Corps	Age		A. S. R.		Overseas Service V-E Day (Months)	
	Withdrawal	Assignment	Withdrawal	Assignment	Withdrawal	Assignment
Medical Corps	45 or over	44 or under	75 or over	74 or under	12	0
Dental Corps	40 or over	39 or under	50 or over	49 or under	6	0
Medical Administrative Corps	40 or over	39 or under	50 or over	49 or under	6	0
Sanitary Corps	40 or over	39 or under	50 or over	49 or under	6	0
Veterinary Corps	40 or over	39 or under	50 or over	49 or under	6	0
Army Nurse Corps	40 or over	39 or under	30 or over	29 or under	6	0
Physical Therapists Corps	40 or over	39 or under	30 or over	29 or under	6	0
Medical Department Dietitians	40 or over	39 or under	30 or over	29 or under	6	0

after such personnel had been returned to the United States, to take up assignments in the United States and help carry the peak load or to serve as replacements for individuals to be sent to the Pacific so that the latter could return its high score personnel to the United States for separation.

The keynote to the separation policy was therefore to give consideration to the participation of all theaters and to be certain that the surplus theaters—European and Mediterranean—would return their personnel at the earliest possible moment. At the end of World War I, with the war terminating for all at the same time, demobilization could be haphazard and yet substantially equitable: Off the gang plank and out. Such a procedure after V-E Day would have been unthinkable. There was a complication over and beyond the necessity of including the Pacific and providing for its participation in any separation plan. As was true of redeployment, military necessity had to govern and take precedence over any individual's score. The keynote to the efficient medical service in this war has been the careful marshaling of the limited number of key specialists who, despite every effort that has been made to utilize their skills to the full, have proved insufficient in number.

The separation plan of the Surgeon General had to deal, therefore, not only with numbers but also with classes of personnel. On the basis of detailed studies it was decided that it would be best to establish two classes—one for scarce specialists, the other for nonscarce specialists and general duty officers—and to set a definite score for each, so as to keep under strict control the outflow of scarce specialists. Consideration was given at one stage of the planning to prohibit the release of any officers in the scarce class, but it was believed better to plan where possible to release very high score individals as well as those over 50 years of age, irrespective of specialty, so long as the number of such releases would not endanger the efficiency of the medical service. The list of scarce specialists was kept to a minimum, after a review of worldwide requirements and availabilities.

Although readjustment regulations place responsibility on the Chief of each Technical Service for the establishment of separation policies, the Surgeon General felt it incumbent on him to establish a representative Separations Board and to charge this board with developing a series of objective criteria which would insure the continuation of high medical standards during the Pacific war and, at the same time, provide an equitable basis for the separation of surplus officers. The Deputy Surgeon General was designated Chairman of the Separations Board, and representatives of the three major forces—Army Air Forces, Army Ground Forces and Army Service Forces—were made members of the Board.

Establishment of Separations Board

The Board thoroughly explored all aspects of the separation policy and had at its disposal comprehensive statistical material before deciding the criteria for separation.

The Board decided to establish definite criteria for separation, subject, as above stated, to the limits of military necessity which governs all discharge policy. These criteria, therefore, create no vested right in any officer to discharge but constitute the goal to be sought, and the general rules to be applied in the absence of supervening military necessity. Such necessity may exist as to the time when, in any individual case, this step can be taken. Also it may arise from the possible need for a relatively few officers with irreplaceable experience whose usefulness is so great as to transcend individual consideration. Separations will be considered by the Surgeon General's Office and granted within the above principles wherever possible. The criteria hereafter set forth and all provisions of the present statement of separation policy must be read and understood as subject to the above qualifications.

Criteria for Separation from the Service

1. Medical Corps officers returned by a theater or declared surplus by a major force (except those with primary military occupational specialties listed in paragraph below) are eligible for release from active duty if their Adjusted Service Rating is 100 or above.

2. Medical Corps officers in certain scarce military occupational specialties are eligible for release from active military duty if they have an Adjusted Service Rating of 120 or more:

Gastroenterology	**Neuropsychiatry**
Ophthalmology and Otolaryngology	**Neurosurgery**
Cardiology	**Thoracic Surgery**
Dermatology	**Plastic Surgery**
Allergies	**Orthopedic Surgery**
Anesthesia	**Clinical Laboratory**

3. Medical Corps officers over 50 years of age, irrespective of their specialty classification, are eligible for relief from active military duty if they are returned to the United States by a theater or declared surplus by a major force.

4. No Medical Corps officer with an efficiency index of 41 or more who desires to remain on active military duty will be relieved, irrespective of age, military occupational specialty or Adjusted Service Rating.

Paragraph four is in keeping with the spirit of readjustment regulations which provide that individuals who desire to remain on active duty will be given every consideration.

Because of the fact that the general hospitals in the United States are now at peak and because the Surgeon General desires to send replacements to the Pacific as quickly as possible, the age provision is not being put into effect at the moment for personnel in the Army Service Forces, and *no Medical Corps officers in the nonscarce category is being released who has less than 110 points (except those who returned from overseas since V-E Day).* However, it is hoped that when more of the surplus personnel is returned from the European and the Mediterranean theaters, this temporary expedient can be lifted.

Subject to the general qualifications stated, the accompanying table summarizes the criteria for separation established for all Medical Department Corps.

Criteria for Separation

Corps	*Age*	*A. S. R.*
Medical Corps*	50 or over	100 or over
Dental Corps	45 or over	100 or over
Medical Administrative Corps	45 or over	90 or over
Sanitary Corps	45 or over	90 or over
Veterinary Corps	50 or over	110 or over
Army Nurse Corps†	40 or over	65 or over
Physical Therapists Corps†	50 or over	65 or over
Medical Dietitians Corps†	50 or over	65 or over

* Scarce categories, A. S. R. 120.

† The following additional provisions cover separations: dependent children under 14; married to demobilized allied personnel.

As in the case of Medical Corps officers, the Army Service Forces, for the time being, have not placed into effect the age provision for Dental Corps officers, and they are operating under a score of 110. But it is hoped that this exception can be removed later.

The foregoing criteria outlined have been established for an initial period of several months, and the point score will be reduced when the number of surplus personnel returned from the European and the Mediterranean theaters makes this possible.

During recent weeks every effort has been made to speed the return of surplus personnel from the European and Mediterranean theaters so that a maximum number of Medical Department officers, especially Medical Corps officers, can be returned to the United States for reassignment and separation.

Although the original plans provided that the last of the surplus personnel would not be returned until the middle of 1946, it now appears probable that the entire surplus will be in this country shortly after the end of 1945. The major factors influencing the return of personnel from the Mediterranean and European theaters are the rate at which troops leave those theaters and the availability of shipping for the

return of Medical Department personnel. So long as large numbers of troops remain, a part of the surplus personnel must remain to furnish them medical care.

The rates at which Medical Corps and other Medical Department officers are separated are conditioned largely by the Pacific. If the Pacific did not exist, or if it could be ignored, as it clearly cannot, separations could be accelerated by approximately five months or more. When a surplus officer with a high score returns from Europe, he could be discharged. But if there are individuals with higher scores in the Pacific, a different procedure is indicated. The officer returning from the European theater, instead of being separated upon arrival, is granted a thirty day leave, plus an allowance for travel time from the port to home and from home to his new station. The individual who has not yet been overseas is granted a preembarkation leave of approximately fifteen days, which, when added to his travel time to the port and the period preparatory to sailing, amounts to approximately one month. Here we have two months. The trip overseas requires just under a month, or a total of three months. Travel time from the port to the new station in the Pacific, overlap on the job and travel time to the port of the officer returning to the United States eat up another month, or a total of four months. The trip home requires another month, or a total of five months. This is the minimum if the officer is separated on arrival. But if his points should be below those of an officer currently assigned in the United States, the process continues. The officer returning from the Pacific will receive a month's leave, additional travel time to and from his home, and only after he has been at his new station for approximately two weeks will the high score individual be released for separation. Here we had a total of seven months. Equity in separations means delay in separations of between five and seven months. Here is the explanation for the apparent paradox of how it happens that two months after V-E Day surplus medical personnel is just beginning to be released from the Army and why it will take many months before all of the surplus is finally separated. However, it is the Surgeon General's firm belief that the American public and the entire medical profession feel that the War Department's basic program of readjustment which includes the Pacific is sound and just.

Within the limitations of logistical requirements, especially transportation, the plan contemplates that the Army will point toward a reduction in the strength of the Medical Corps by approximately 7,000 by May of 1946. Because of the need to absorb the leave and travel time of replacements to the Pacific, not more than 4,000 of this number can be separated by the end of this year.

The transfer of several hundred thousand medical personnel in the midst of war, under great urgencies, involving three continents, represents the single largest undertaking of its kind in the history of the world and is dwarfed only by the still greater transfer involved in moving all Army personnel. To cope with this situation of unparalleled magnitude, the Surgeon General has evolved, after the most careful consideration, a detailed plan which he believes will secure the end desired by all—the finest medical service for the American soldier and the highest degree of equity for the officers and men of the Medical Department who are provided this service.

ARMY AWARDS AND COMMENDATIONS

Lieutenant Colonel Manuel E. Lichtenstein

Lieut. Col. Manuel E. Lichtenstein, formerly of Chicago, was recently awarded the Brazilian decoration "Medal de Guerra." The presentation was made by General Mascarenhas on May 29, 1945 in the name of the President of Brazil. Dr. Lichtenstein organized the medical staff of the Brazilian expeditionary force assigned to an evacuation hospital and successfully established the practice of modern surgical methods for the care of battle casualties among Brazilian troops during the Italian campaign. Dr. Lichtenstein is also the recipient of the Bronze Star (THE JOURNAL, April 21, 1945, p. 1059). He graduated from Rush Medical College, Chicago, in 1925 and entered the service Oct. 15, 1942.

Major Brendan P. Phibbs

For meritorious service in supervising and aiding in the organization for the evacuation of the wounded, Major Brendan P. Phibbs, formerly of Winnetka, Ill., was recently awarded the Bronze Star. As a surgeon with the headquarters of the combat command battalion of the 12th Armored Division, Major Phibbs frequently exposed himself to enemy fire to see that evacuation was accomplished expeditiously and by the safest routes. Dr. Phibbs graduated from Northwestern University Medical School, Chicago, in 1942 and entered the service in June 1942.

Captain Sherwood P. Burr Jr.

Capt. Sherwood P. Burr Jr., formerly of Eugene, Ore., was recently commended by Major Gen. Robert Douglass, commanding the 7th A. A. F., for his work with the 11th bombardment group, which participated in almost every major move of the offensive that has rolled the Japanese back more than 3,000 miles. Dr. Burr graduated from the University of Oregon Medical School, Portland, in 1939 and entered the service Sept. 5, 1941.

Major Leonard S. Shemanski

Major Leonard S. Shemanski, formerly of Menasha, Wis., was recently awarded the Bronze Star for "meritorious achievement in connection with military operations against the enemy in Luzon, Panay and Negros, Philippine Islands, from Jan. 9, 1945 to May 1, 1945." Dr. Shemanski graduated from Marquette University School of Medicine, Milwaukee, in 1934 and entered the service July 15, 1941.

Captain George C. Blanchard Jr.

Capt. George C. Blanchard Jr., formerly of Augusta, Ga., was recently awarded the Bronze Star. The citation accompanying the award reads, in part, "Captain Blanchard, a battalion surgeon, was faced with the problem of setting up an advanced aid station in Strass, Germany, to take care of a large number of wounded infantrymen while the town and approaches to this town were yet under heavy shell fire. Vehicles which had attempted to get into the town, including tanks, had been knocked out and evacuation was impossible, initially. To minimize suffering and to prevent all possible loss of lives, Captain Blanchard made his way into the town before all the enemy resistance had been reduced. He was unable to find time to rest for many hours. His action saved the lives of many and his action is a credit to the medical profession and to the service." Dr. Blanchard graduated from Cornell University Medical College, New York, in 1942 and entered the service July 3, 1943.

Captain John B. Condon

Capt. John B. Condon, formerly of Chicago, was recently awarded the Bronze Star "for meritorious service in connection with military operations against the enemy from Feb. 4, 1945 to Feb. 12, 1945 in France, while located at Fortschwihr, when the clearing station under Captain Condon's command was forced to operate considerably under strength. Casualties required the constant care of this medical officer, and exceedingly adverse weather conditions added considerably to Captain Condon's problems, as he was forced to operate in tents. The superior performance of duty rendered by this officer reflects great credit on himself and on the Medical Corps." Dr. Condon graduated from Loyola University School of Medicine, Chicago, in 1940 and entered the service Jan. 5, 1943.

Captain George A. French

The Silver Star was recently awarded to Capt. George A. French, formerly of Appleton, Wis., for gallantry in the European theater, April 4, "when he advanced across a bridge under direct enemy observation and a rain of fire to care for the wounded until evacuation was possible." Dr. French graduated from Marquette University School of Medicine, Milwaukee, in 1942 and entered the service Aug. 11, 1943.

VETERANS

OUTPATIENT TREATMENT FOR VETERANS

Thirty-one mental hygiene clinics and intensive treatment courses in nineteen neurosis centers connected with general medical and surgical hospitals have been authorized by Brig. Gen. Frank T. Hines, Administrator of Veterans Affairs, for the outpatient treatment of veterans with service connected disabilities. The clinics will make treatment readily available to veterans disabled in service who are in need of reorientation and will aid the veteran in returning to normal life and a gainful occupation in the shortest time possible. The outpatient clinics will be located at the following hospitals or regional offices: Boston; Hartford, Conn.; New Orleans; Cleveland; New York; Pittsburgh; Providence, R. I.; St. Louis; Washington, D. C.; Louisville, Ky.; Minneapolis; San Francisco; Atlanta, Ga.; Cincinnati; Dearborn, Mich.; Indianapolis; Newark, N. J.; Milwaukee; Denver; Jackson, Miss.; Seattle; Huntington, W. Va.; Bay Pines, Fla.; Columbia, S. C.; Des Moines, Iowa; Omaha; Memphis, Tenn., and Batavia, N. Y., though this clinic may be in either Syracuse or Buffalo.

Neurosis centers will be located at Aspinwall (Pittsburgh); Atlanta, Ga.; Batavia, N. Y.; Bay Pines, Fla.; Brecksville (Cleveland); Bronx (New York); Des Moines; Fort Howard, Md.; Hines (Chicago); Huntington, W. Va.; Indianapolis; Jefferson Barracks (St. Louis); Kecoughtan, Va.; Portland, Ore.; Minneapolis; San Francisco; West Roxbury (Boston), and Wood (Milwaukee).

Each outpatient clinic will be fully equipped for diagnosis and treatment, with facilities on hand for x-ray and clinical laboratory examination. The neurosis centers will be equipped for intensive therapy of the severely affected neuropsychiatric patient and will have available equipment for therapy embracing psychotherapy both for the individual and for the group; narcoanalysis and hypnotism for the purpose of exploring the subconscious in the same manner used in Army and Army Air Forces hospitals abroad for the treatment of the severely affected psychoneurotic.

In both types of clinic occupational therapy, psychotherapy, recreational therapy and social services, all aimed at an early reestablishment of the veteran in his home community, will be provided.

The clinics and neurosis centers will be placed in operation just as rapidly as qualified personnel can be obtained. Some psychiatrists and other personnel have been attending courses in the Army's Mason General Hospital, Long Island, N. Y., and other personnel is being sought by the Veterans Administration through recruitment.

ARMY

A VOICE FOR THE BATTALION SURGEON

To the Editor:—I would appreciate the following being printed. With the consideration to Major Gen. P. R. Hawley's open letter "Correspondence Concerning the Medical Department," in the Medical Bulletin ETO Number 30, April 1945, I feel that I can speak for my colleagues, the battalion surgeons, many of whom have endured the yoke far longer and with better grace and equanimity than I.

The Medical Department has done a wonderful job during the emergency. Those of us who came in as reserve officers early in 1942 realized the urgency of our then precarious military position and cooperated fully. Troop units had to be manned with competent agreeable and vigorous doctors. There is admittedly nothing professional about the work of a doctor with troops. The work is further complicated by manifest and deliberate attempts on the part of some low moral calibered soldiers to shirk their attendant responsibilities in the line. Moreover, the lack of apparatus for diagnosis, the uncertainty of supply, the desire of some commanders to delimit the size of sick call by devious means, including coercion and the threat of extra duty, plus the pitiful dependence of the first echelon surgeon on rear echelons who are inclined to look down their noses on this poor relation colleague who so rarely can make the correct anatomic and pathologic diagnosis, being without the instruments, x-rays or laboratory facilities for such, makes the first echelon medical officer bitter in time, especially since, having done so much with so little for so long, he becomes indispensable in this assignment and is never made available when and if in his meager opportunity to associate in professional channels he does meet a former teacher colleague or class mate who is in a position to offer a more fertile field for professional endeavor.

The ultimate control of the military destiny of a medical officer by a field officer is unjust. The practice of keeping medical officers either in hospitals or in field units is unjust, more especially when the time period concerned runs into its fourth year. I realize that any medical officer can do well in a hospital. I also realize that many medical officers cannot do well in the field, either through defects in health or by deliberate misapplication. I realize too that the talents of many true specialists would be wasted in such field units and I do not contemplate such waste. I speak only for that horde of little men whose professional, political and military friends are not highly placed: those young men with excellent education, training and military records of efficiency behind them who, because of a T. O., can never rise higher in rank, who because of being members of A. G. F. are not eligible for transfer to hospital units of the A. S. F. I speak of men who can only lose professional skill by this enforced, and now after three full years, unwilling further retention in that type of medical service which many younger men could carry out to much better military advantage. I speak of those men who, when they return to civilian practice, will return at a great professional disadvantage from pure lack of association, lack of opportunity for doing and seeing and reading, engendered almost entirely by a short sighted policy of assignment, reassignment and rotation, which no belated special superficial and impersonal refresher course will ever to able to overcome.

WALTER E. VOGT JR., CAPTAIN, M. C., A. U. S.

NOTE.—The communication of Capt. Walter E. Vogt Jr. has been discussed with various leaders in the field of military medical services. The consensus seems to be that the ordinary young doctor without special training can be rotated. The young man who has had two or three years of residency in a specialty is more valuable to the patient than one without such training and is therefore more valuable to the Army Medical Department for services in its specialized hospitals. Since hospitals are, for the most part, staffed with trained men, only general practitioners are left for purposes of rotation. Years of experience have shown that it is impossible to place any physician in a front line unit without training in a number of subjects which are never taught in medical schools. These have to do with the subjects of self protection under fire, cooperation with troops and similar matters. Medical officers in general cannot agree with the statement of Captain Vogt that "there is admittedly nothing professional about the work of a doctor with troops." If this was true the Army could easily put lawyers and railway engineers in positions now occupied by many physicians. Even men especially trained under medical leadership as first aid assistants find certain medical conditions which require the personal attention of a physician.—ED.

NEW CHIEF AT VALLEY FORGE

Lieut. Col. Steige D. Blackford, Charlottesville, Va., was recently appointed chief of the medical service at Valley Forge General Hospital, Phoenixville, Pa. He succeeds Lieut. Col. Maurice A. Schitker, Toledo, Ohio, who has left for an overseas assignment.

Colonel Blackford recently returned to this country after thirty months' service as chief of the medical service of the 8th Evacuation Hospital in North Africa and Italy. He was awarded the Legion of Merit for his work with that hospital.

ORGANIZATION SECTION

PROPOSED FEDERAL PROGRAMS TO PROMOTE SCIENTIFIC RESEARCH

An Analysis of Legislation Pending in the Seventy-Ninth Congress

Prepared by the Bureau of Legal Medicine and Legislation, American Medical Association

Identical bills are pending in the Senate and the House of Representatives to implement the recommendations contained in the report recently submitted to President Truman by Dr. Vannevar Bush, director of the Office of Scientific Research and Development, and other collaborating scientists, outlining a suggested federal program to promote scientific research. The Senate bill, S. 1285, introduced on July 19 by Senator Magnuson of Washington, was referred to the Senate Committee on Commerce, of which Senator Bailey of North Carolina is chairman. The House bills, H. R. 3852, introduced on July 19 by Representative Mills of Arkansas, and H. R. 3860, introduced on July 20 by Representative Randolph of West Virginia, have been referred to the House Committee on Interstate and Foreign Commerce, of which Representative Lea of California is chairman.

On July 23 Senator Kilgore of West Virginia, for himself and Senator Johnson of Colorado, and Senator Pepper of Florida, introduced S. 1297, which embodies principles which the Subcommittee on War Mobilization of the Senate Military Affairs Committee, on the basis of extensive studies made over the past two years, has set up as desirable in any legislation designed to meet the postwar scientific needs of the nation. The bill is pending in the Senate Committee on Military Affairs, of which Senator Thomas of Utah is chairman.

Representative May of Kentucky has introduced another bill relating to scientific research, H. R. 3440. This bill would authorize an appropriation of not to exceed $8,000,000 annually to enable the National Academy of Sciences, through a research board for national security consisting of representatives of the Army, Navy and civilians of outstanding accomplishments, to provide for scientific research and advancement determined by the board to be desirable in the interest of national security. It has passed the House of Representatives and is pending in the Senate Committee on Naval Affairs.

Another pending bill, S. 825, was introduced by Senator Byrd of Virginia on April 4 and was referred to the Senate Committee on Naval Affairs, of which Senator Walsh of Massachusetts is chairman. It would create a Research Board for National Security to include representatives of the Army and Navy, the chairman of the National Advisory Committee for Aeronautics and civilian scientists, engineers or industrialists. It will be the duty of the board to formulate programs of scientific research and development relative to problems of national security. The term "science" as used in the bill includes the employment of scientific methods of analysis, experiment and test in any "branch of science or technology, including engineering, medicine, dentistry, psychology and biology." This bill was favorably reported to the Senate July 28, with amendments.

Another bill has been introduced in the Senate by Senator Fulbright, Arkansas, S. 1248. It proposes to establish a Bureau of Scientific Research in the Department of Commerce "to aid, encourage, and protect the research and enterprise of inventors, scientists, technicians, scientific and educational institutions, and research laboratories engaged in scientific and technical work, and to make their resultant discoveries and data more readily available, without discrimination, to all sections of industry, agriculture, and the public in order to promote full employment and higher standards of living." This bill is pending in the Senate Committee on Commerce, of which Senator Bailey, North Carolina, is chairman.

With the exception of the three bills designed to implement the recommendations contained in the Bush report, these proposals differ in many details; that fact was given recognition by Senator Kilgore at the time he introduced his bill. After referring to the other pending legislation, he expressed the hope that arrangements could be made for joint hearings "so that the issues presented by these different bills can be clarified and agreement reached at an early date on the scope of research needed in the interest of national security and also on the details of organization and administration so essential to the success of any national program of scientific research."

There follows a factual analysis of the Magnuson-Mills-Randolph bill and the Kilgore bill.

THE MAGNUSON-MILLS-RANDOLPH BILL

This legislation would create a National Research Foundation as an independent agency in the executive branch of the government to secure the full development and application of the nation's scientific and technical resources for national defense, prosperity, health and welfare.

Administrative Board.—The powers and duties of the foundation will be exercised by a board of nine members appointed by the President without regard to political affiliations and solely on the basis of their demonstrated interest in and capacity to promote the purposes of the foundation. The board will be authorized to employ a director at a salary of $15,000 a year, who will be the principal executive officer of the foundation. Two deputy directors may be appointed by the director, each of whom will receive compensation at the rate of $12,000 a year. The members of the board will serve without compensation but will be allowed actual and necessary traveling and subsistence expenses when engaged, away from home, in the duties of their office.

Divisions Within Foundation.—Within the foundation there will be a minimum of five divisions as follows: (1) a Division of Medical Research to carry out programs relating to research in biologic science, including medicine and the related sciences; (2) a Division of Physical Sciences to carry out programs relating to research in the mathematical and physical sciences; (3) a Division of National Defense to carry out programs relating to scientific research on military matters; (4) a Division of Scientific Personnel and Education to carry out the program relating to the grant of scholarships and fellowships in the mathematical, physical and biologic sciences, and (5) a

Division of Publications and Scientific Collaboration to carry out programs relating to the public dissemination of scientific information among scientists. Additional divisions may be created by the board.

Committees Within Divisions.—In each division will be a committee of not less than five members appointed by the board after receiving recommendations from the National Academy of Sciences. The committee within the Division of National Defense, in addition, will include a member designated by the Secretary of War and a member designated by the Secretary of the Navy.

The appointed members will receive compensation at the rate of $50 a day while engaged in the business of the foundation plus expenses when engaged, away from home, in the duties of their office. Each committee will make recommendations to and advise and consult with the board and the director with respect to matters of its division. Additional powers and duties may be devolved on the committees by the board.

Powers and Duties of the Foundation.—In carrying out the purposes of the bill, the foundation will be authorized and directed:

(1) to develop and promote a national policy for scientific research and scientific education;

(2) to initiate and support basic scientific research and scientific development in the mathematical, physical and biologic sciences through contracts, grants or other forms of assistance;

(3) to initiate and support scientific research and scientific development on matters relating to the national defense through contracts, grants or other forms of assistance;

(4) to discover and develop scientific talent, particularly in American youth;

(5) to grant scholarships and fellowships in the mathematical, physical and biologic sciences;

(6) to foster the interchange of scientific information among scientists in this country and abroad; and

(7) to correlate the foundation's scientific research and scientific development programs with those undertaken by public and private research groups.

Authority of Foundation.—The foundation will be specifically authorized (1) to prescribe such rules and regulations as it deems necessary; (2) to enter into contracts, or amendments or modifications of contracts without legal consideration, without performance or other bonds in the case of all contracts which relate to scientific research or scientific development; (3) to make advance, progress and other payments which relate to scientific research or scientific development; (4) to acquire by purchase or otherwise, hold and dispose of by sale, lease, loan or otherwise real and personal property of all kinds necessary for or resulting from scientific research or scientific development without regard to the provisions of law relating to the acquisition, holding or disposition of property by the United States; (5) to receive and use funds donated by others, provided such funds are donated, without other restriction, in furtherance of one or more of the general purposes of the foundation; (6) to publish or arrange for the publication of scientific and technical information so as to further the full dissemination of information of scientific value consistent with the national interest; (7) to accept and utilize the services of voluntary and uncompensated personnel and to pay the actual and necessary traveling and subsistence expenses, including in lieu of subsistence per diem at a rate not in excess of $10, of such personnel incurred in the course of such services; (8) to prescribe the extent to which vouchers for funds expended under contracts for scientific research and development shall be subject to itemization or substantiation prior to payment, without regard for the limitations of other laws relating to the expenditure of public funds and accounting therefor; (9) to establish a National Science Reserve in which will be enrolled all those who receive scholarships and fellowships in science and medicine from the foundation. Members of the National Science Reserve will be available for call into the service of the government for scientific and technical work in time of war or other national emergency as declared by the Congress or proclaimed by the President.

Appropriations.—The bill will authorize to be appropriated annually to the foundation such sums as may be necessary to carry out its provisions. Funds appropriated for the foundation will, if obligated during the fiscal year for which appropriated, remain expendable for a period of four years. After such a four year period, the unexpended balances will revert to the treasury.

General Provisions.—The bill specifically provides that the foundation shall not itself operate any scientific or technical facilities of its own.

There will be transferred to the foundation all powers, functions and duties of the Office of Scientific Research and Development and its constituent committees. All personnel, property, records, funds, contracts, assets and liabilities of the Office of Scientific Research and Development, and of its constituent committees, will also be transferred to the foundation. This transfer will take effect at such time as the President directs.

Members of the board and members of the committees within the divisions may engage in private and gainful employment, but no compensation for such employment may be received in any form by any such member (1) from any profit-making organization which receives funds under contract, or otherwise, within the cognizance of the division or divisions of the foundation with which such member is concerned or (2) in respect of any particular matter which directly involves the foundation or in which the foundation is directly interested.

The director will be authorized to appoint and fix the compensation of necessary personnel, subject to the provisions of the civil service laws and regulations and the Classification Act of 1923. Technical and professional personnel may be employed without regard to the provisions of the Classification Act. The director, the deputy directors and the members of the committees within the divisions will also be appointed without reference to the civil service laws or the Classification Act.

The foundation will be required to submit an annual report in writing to the President and the Congress and the bill, if enacted, will be cited as the "National Research Foundation Act of 1945."

THE KILGORE BILL

The title of the Kilgore bill, S. 1297, indicates its purpose, namely, to promote the progress of science and the useful arts, to secure the national defense and to advance the national health and welfare.

National Science Foundation.—An independent agency of the federal government to be known as the National Science Foundation will be created. It will be administered by a director appointed by the President, by and with the advice and consent of the Senate. His salary will be $15,000 a year.

The director will be required to consult and advise with a National Science Board on all matters of major policy or program. The board will consist of the director as chairman, the heads of the Departments of War, Navy, Justice, Interior, Agriculture, Commerce and Labor, and the Federal Security Agency or their designees, plus eight public members appointed by the President by and with the advice and consent of the Senate.

Promotion of Research and Development.—The foundation will be required to give particular attention to promoting research and development activities relating to (1) national defense, (2) health and medicine, (3) the basic sciences, (4) the conservation, development and use of the natural resources of the nation, (5) the development of methods and processes beneficial to small business enterprises and (6) the adaptation to peacetime use of wartime research and facilities.

Not less than 20 per cent of the funds to be made available to the foundation for research and development activities will

be expended for research and development in each of the following fields: (1) national defense and security and (2) health and medicine.

The bill requires the foundation to consider the desirability of utilizing facilities available in departments and agencies of the federal government, state and local governments, educational institutions, research institutions, private industrial organizations, and individual scientists particularly qualified to carry out such projects. Not less than 50 per cent of the total funds appropriated by the Congress for research and development activities under the bill must be expended for engaging the facilities of qualified nonprofit educational institutions and research institutions.

Committees Within Foundation.—A minimum of two committees within the foundation are to be established: (1) a Research Committee for National Defense consisting of a chairman to be appointed by the President by and with the advice and consent of the Senate, whose salary will be $12,000 a year, and nine members at large, three to be designated by the Secretary of War, three by the Secretary of the Navy and three by the director with the advice and approval of the board; and (2) a Research Committee for Health and the Medical Services, consisting of a chairman appointed by the President by and with the advice and consent of the Senate, whose salary will be $12,000 a year, and nine members at large, of whom three shall be designated by the administrator of the Federal Security Agency and six by the director with the advice and approval of the board.

The members at large to be appointed by the Secretaries of War and the Navy and the administrator of the Federal Security Agency may be civilian or military employees of the government or public members. The director will be required to advise with these two committees with respect to the formulation of overall research and development programs in the fields of national defense and health and medicine and must secure the approval of the committees with respect to the determination of specific projects and the selection of specific facilities.

Additional advisory committees may be set up by the director, and members of such committees will be appointed by the director by and with the advice and consent of the board and, in appointing such members, the director may request appropriate national scientific organizations to submit panels of candidates from which he may make his selection.

Scholarships and Fellowships.—The foundation will be authorized to grant scholarships and fellowships to persons showing special aptitude, for one year's study at a nonprofit institution of higher education or other nonprofit institution. Scholarships and fellowships are to be renewable for a period up to five years at the option of the foundation.

Survey of Federal Scientific Activity; Dissemination of Research Findings.—The foundation will be required to make and maintain a comprehensive survey of federally financed research and development activities. Any agency engaged in such activities will be required, on request by the director, to furnish whatever data and reports may be needed. The foundation must evaluate such survey data and make recommendations to the President and the agencies concerning improvements.

Each contracting organization or institution or individual, as a condition to receiving financial support from the foundation, will be required to make available full data on all inventions, discoveries and other significant findings. The foundation will be directed to collect, edit, publish and disseminate pertinent data on all inventions, discoveries and other findings resulting from federally financed research and development activities. It must take such steps as necessary to disseminate such data to the public, including the preparation of abstracts, translations, bibliographies and microfilm reproductions of research and development reports and publications.

The foundation will be required to do what it can to eliminate restraints on the free expression of scientific truths and to insure ample freedom in the exercise of creative talents and in the development of promising new ideas in connection with all research and development projects promoted, financed or otherwise supported by the federal government.

All materials or equipment purchased or furnished by federal funds in connection with research and development projects, and any invention, discovery or finding resulting from such federally financed projects shall be the property of the federal government.

Restriction on Dissemination of Information.—The Defense Committee must declare secret or restricted any scientific or technical information, data, patents, inventions or discoveries in or coming into the possession or control of the foundation, the secrecy or restriction of which the President or his designee or designees certify as being essential in the interest of national defense.

Patents.—The director will be required to patent all significant inventions or discoveries resulting from research and development projects. Any citizen, corporation or other organization desiring to use any invention, discovery or patent which is or may hereafter become the property of the United States will, on proper application, be granted without further limitation a nonexclusive license for which there will be no charge. The foundation will be required, however, to refuse to grant a license to any applicant on a finding in writing by the Department of Justice to the director that the granting of such license will tend to promote or result in a monopoly or a practice which is in restraint of trade.

Appropriations.—Such sums as may be necessary to carry out the provisions of the bill may be annually appropriated by the Congress to the foundation. In addition, the foundation may solicit and receive financial grants, personal services and any other aid furthering scientific and technical progress, may enter into contracts and make expenditures for personnel, equipment and services as it may deem necessary. The foundation may not itself or through its own employees operate any laboratories, pilot plants or other such scientific or technical facilities which it may acquire.

Employment of Personnel.—The director will be authorized to appoint and fix the compensation of necessary personnel. Appointments and compensation shall be made in accordance with the provisions of the civil service laws and the Classification Act, except that technical and professional personnel may be employed without regard to such laws.

Public members of the board and of any advisory committee will serve without remuneration except for per diem allowances, transportation and other necessary expenses incurred. No employee of the foundation or member of any advisory committee may participate in any decision or recommendation affecting his personal financial interest or the activities of any organization in which he has a financial interest or by which he is employed.

"Research and Development" Defined.—These terms are declared to mean not only theoretical analysis, exploration and experimentation but also the extension of investigative findings and theories of a scientific or technical nature into practical application, including the preparation of plans, specifications and standards for various goods and services, the undertaking of related economic and industrial studies, the experimental production and testing of models, and the building and operation of pilot plants.

Miscellaneous.—The director must render an annual report in writing to the President and to Congress, summarizing the activities of the foundation and containing such recommendations as he may deem appropriate. The foundation will be granted the free use of the mails. As used in the bill, the term "federally financed" means financed in whole or in part by the federal government. The bill, if enacted, will be cited as the "National Science Foundation Act of 1945."

THE MATERNAL AND CHILD WELFARE ACT OF 1945

An Analysis Prepared by the Bureau of Legal Medicine and Legislation, American Medical Association

Senator Pepper, Florida, for himself and nine other members of the Senate Committee on Education and Labor, has introduced a bill, S. 1318, to provide for the general welfare by enabling the several states to make more adequate provision for the health and welfare of mothers and children and for services to crippled children and for other purposes. Joining Senator Pepper in sponsoring this legislation were Senator Walsh, Massachusetts; Senator Thomas, Utah; Senator Hill, Alabama; Senator Chavez, New Mexico; Senator Tunnell, Delaware; Senator Guffey, Pennsylvania; Senator LaFollette, Wisconsin; Senator Aiken, Vermont, and Senator Morse, Oregon. The bill was referred to the Senate Committee on Education and Labor, of which Senator Murray, Montana, is chairman.

An appropriation of $100,000,000 will be authorized for the fiscal year ending June 30, 1946: $50,000,000 earmarked for maternal and child health services, $25,000,000 for services for crippled children, $20,000,000 for child welfare services and $5,000,000 for expenses necessary to enable the Children's Bureau to administer the provisions of the bill and to develop and promote effective measures for carrying out its purposes, including "studies, demonstrations, investigations and research, the training of personnel for federal, state and local service, and the payment of salaries and expenses of personnel detailed at the request of state agencies to cooperate with and assist such agencies" in carrying out the objectives of the legislation. Thereafter such sums will be made available as the Congress shall decide.

The bill, which Senator Pepper has described as "a modest beginning," has five titles:

TITLE I. MATERNAL AND CHILD HEALTH SERVICES

The stated objectives of this title are to provide and maintain services and facilities to promote the physical and mental health of mothers during the maternity period and of children, including medical, nursing, dental, hospital and related services and facilities required for maternity care, preventive health work and diagnostic services for children, school health services, care of sick children, and correction of defects and conditions likely to interfere with the normal growth and development and the educational progress of children. The development of more effective measures for carrying out the purposes of the title is contemplated, including demonstrations and the training of personnel for state and local maternal and child health services.

Of the total appropriation to be made available under this title, $5,000,000 will be allotted by the Secretary of Labor to the several states, and allotments must be matched dollar for dollar by state or state and local funds. In determining what amount each state shall be allotted, the Secretary of Labor will take into consideration the number of children under 21 years of age in such state in relation to the total number of children under 21 years of age in the United States.

The remainder will be allotted to the states by the Secretary of Labor after taking into consideration for each state such factors as the number of mothers and children under 21 years of age in the state for whom the services and care are to be made available, and the cost of furnishing such services and care to them, the special problems of maternal and child health and the financial need of the state for assistance in carrying out the state plan.

Approval of State Plans.—Allotments will be paid to those states whose plans for developing programs and for providing care and services have been approved by the chief of the Children's Bureau. In order for a plan to be approved by the chief of the Children's Bureau, it must:

1. Provide for financial participation by the state.

2. Provide for a statewide program or for extension of the program each year so that it will be in effect in all political subdivisions by July 1, 1955.

3. Provide that services and facilities shall be available to all mothers and children in the state or locality who elect to participate in the benefits of the program. There must be no discrimination because of race, creed, color or national origin, and no residence requirements.

4. Provide for the administration of the plan by the state health agency, or for the supervision of the administration of the plan by the state health agency, and for appropriate coordination of the plan with the general public health and medical care program of the state health agency which will be authorized to develop agreements or cooperative arrangements with other state or local public agencies whose functions include the provision of services similar or related to those furnished under the state plan.

5. Be made part of the state plan for maternal and child health services submitted in accordance with the provisions of title V, part 1, of the Social Security Act.

6. Provide effective methods of administration, including the establishment and maintenance of personnel standards on a merit basis, standards for professional personnel rendering medical, dental, nursing and related types of care or service, and standards for hospital and other institutional care and services. Standards are to be established by the state health agency after "consultation" with professional advisory committees appointed by the state health agency. Mothers and children, or persons acting in their behalf, will be permitted to select, from among those meeting standards prescribed by the state health agency, the physician, hospital, clinic or health service agency of their choice. Where no such selection is made, the state plan must set forth the method by which the care will be made available. The bill provides that the physician, hospital, clinic or health service agency selected may refuse to accept the case.

A state plan must provide for adequate remuneration for the persons and institutions providing medical care and related services, must provide opportunities for postgraduate training of professional and technical personnel, and for such use of health centers, hospitals, clinics and health service agencies, public and voluntary, as will achieve the satisfactory distribution and coordination of preventive, diagnostic, consultative and curative services provided by general practitioners, specialists, public health personnel, laboratories and others.

A state plan must provide payments to individual physicians for care furnished under this title on a per capita, salary, per case or "per session" basis or, in the case of consultations or emergency visits, on a fee-for-service basis. A state plan must furthermore provide for the purchase of care from public or voluntary hospitals and other health service agencies included under the state plan on a basis related to cost for providing the care.

7. Provide for adequate dissemination of information with regard to the maternal and child health services to be made available under this title.

8. Provide for reports to the chief of the Children's Bureau.

9. Provide for cooperation with medical, health, hospital, nursing, education and welfare groups and organizations in the state.

10. Provide (*a*) for a general advisory council appointed by the state health agency and composed of members of the professions or agencies, public and voluntary, that furnish care or services under the state plan, and other persons representing the public who are informed on the need for and problems related to the provision or receipt of maternal or child health services and medical care of mothers and children, and (*b*) for technical advisory committees appointed by the state health agency composed of medical and other professional groups concerned with the administration or operation of a state plan. If the state health agency administers a program for services to crippled children, the same general advisory council shall serve both the maternal and child health and the crippled children programs.

11. Provide for a fair hearing before the state health agency for any mother or other person acting in behalf of a child whose claim for services is denied or for any physician or other person, organization or institution participating or desiring to participate in furnishing services or facilities under the plan.

Federal Advisory Committees.—The chief of the Children's Bureau will formulate general policies for the administration of this title after "consultation" with a conference of state health officers and an advisory committee composed of professional and public members and, as necessary, technical advisory committees which "he" shall appoint.

TITLE II. SERVICES FOR CRIPPLED CHILDREN

The stated objectives of this title are to enable each state to provide and maintain services and facilities for the care and treatment of children who are crippled, otherwise physically handicapped or suffering from conditions which lead to crippling or physical handicaps, including services for locating such children, for providing medical, surgical, corrective and other services and care, and facilities for diagnosis, hospitalization and after-care for such children. Demonstrations and the training of personnel for state and local crippled children's services are contemplated.

Out of the total appropriation authorized under this title, the Secretary of Labor will allot to each state such part of $2,500,000 as he finds that the number of children under 21 years of age in such state bore to the total number of children under 21 years of age in the United States in the latest calendar year for which the Bureau of the Census has available statistics. Such allotments must be matched dollar for dollar by state or state and local funds made available for services for crippled children.

The remainder of the appropriation will be allotted to the states by the Secretary of Labor after taking into consideration for each state such factors as (1) the number of crippled children under 21 years of age in the state for whom services and care are to be made available and the cost of furnishing such services and care to them, (2) the special problems of crippled children and (3) the financial need of the state for assistance in carrying out the state plan.

Approval of State Plans.—Allotments will be made to the states which have submitted to and had approved by the Children's Bureau state plans for developing programs for crippled children. As in the case of state plans developed under title I, the bill indicates the contents a state plan must have to be approved. Such a state plan for services for crippled children must meet essentially the same requirements specified for plans developed under title I except that, if a state agency other than the state health agency is designated by state law to administer the program for crippled children, that agency may continue as the state administrative agency until July 1950, after which the state health agency must have jurisdiction. Services to be provided under this title must be available to all crippled children without regard to financial status, race, creed, color or national origin, and there may be no residence requirement. Individual physicians will be paid as indicated in title I, except that title II makes no provision for payment on a per capita basis.

Federal Advisory Committees.—The chief of the Children's Bureau will formulate all general policies for the administration of this title after "consultation" with (1) a conference of executive officers of state agencies administering the program for crippled children under this title and (2) an advisory committee composed of professional and public members and, as necessary, technical advisory committees, which "he" shall appoint.

TITLE III. CHILD WELFARE SERVICES

The declared purpose of title III is to assist each state public welfare agency to develop effective statewide child welfare programs and measures, including the training of personnel, for extending and strengthening public child welfare services, and for providing suitable care and protection for children without parental care and supervision, and children who are dependent, neglected or delinquent, or in danger of becoming neglected or delinquent.

For each of the fiscal years ending June 30, 1946 and June 30, 1947 the Secretary shall allot to each state such part of $10,000,000, and for the fiscal year ending June 30, 1948 and for each fiscal year thereafter such part of three fourths of the total amount appropriated for child welfare services as he finds that the number of children under 21 years of age in such state bore to the total number of children under 21 years of age in the United States in the latest year for which the Bureau of the Census has available statistics. Such allotments must be matched dollar for dollar by state or state and local funds made available for child welfare services.

For the fiscal year ending June 30, 1946 and for each fiscal year thereafter the remainder of the sum appropriated for child welfare services will be allotted to the several states by the Secretary of Labor, taking into consideration for each state such factors as (1) the number of children under 21 years of age in the state for whom child welfare services are to be made available and the cost of providing such services and care to them, (2) the special problems of child welfare and (3) the financial need of the state in carrying out the state plan.

Approval of State Plans.—Allotments will be made to states which have submitted to and had approved by the Children's Bureau state plans for child welfare services. The chief of the Children's Bureau will be required to approve any state plan which meets the following conditions:

(1) Financial participation by the state.

(2) A statewide program, including at least guidance and social service to or in behalf of children who are dependent, neglected or delinquent, or in danger of becoming neglected or delinquent, or for the extension of the program each year so that such guidance and service will be available to all children in need thereof, in all political subdivisions of the state not later than July 1, 1955.

(3) Services and care furnished under the plan must be made available to all children without regard to financial status, race, creed, color or national origin, and without residence requirements.

(4) Administration or supervision of the plan by the state public welfare agency and coordination of the plan with the general public welfare program of the state public welfare agency which will be authorized to develop agreements or cooperative arrangements with other state agencies whose functions include the provision of services related to the services furnished under the state plan.

(5) The state plan must be made a part of the plan for child welfare services submitted in accordance with the provisions of title V, part 3, of the Social Security Act.

(6) The plan must provide such methods of administration as are found by the chief of the Children's Bureau to be necessary for the proper and efficient operation of the plan, including methods relating to the establishment and maintenance of personnel standards on a merit basis.

(7) The state public welfare agency must make such reports in such form and containing such information as the chief of the Children's Bureau may from time to time require.

(8) Appropriate cooperation must be provided for with state and local agencies, public and private, concerned with child health, education, child welfare and related subjects.

(9) The plan must provide for a program of training for personnel rendering child welfare services.

Definitions.—As used in this title, the term "child welfare services" means (1) guidance and social service to or on behalf of children who are dependent, neglected or delinquent, or in danger of becoming neglected or delinquent; (2) placement, supervision and maintenance of children in foster family homes; (3) temporary care of children who are dependent, neglected or delinquent, or in danger of becoming neglected or delinquent, especially in areas where children would otherwise be detained in jail or would be deprived of necessary protection and shelter or study of their special needs; (4) specialized services needed to strengthen and improve the programs of public institutions caring for children; (5) care in foster homes or day care centers for children whose mothers are employed or whose home conditions require care outside their own homes during any part of the twenty-four hour day, including services necessary to

assure proper use of day care facilities and to safeguard children receiving care; (6) payment of the cost of returning nonresident children to their own communities; if such return is desirable and the cost thereof cannot otherwise be met, and (7) cooperation with state and community agencies in improving conditions affecting the welfare of children.

TITLE IV. ADMINISTRATION

If the Secretary of Labor finds that in the administration of any plan approved under the bill there is a failure to comply substantially with any requirement specified as necessary for inclusion in a state plan, he may withhold further allotments.

The Children's Bureau will be directed to make and aid the financing of such studies, demonstrations, investigations and research as will promote the efficient administration and operation of the legislation.

TITLE V. GENERAL PROVISIONS

The chief of the Children's Bureu, subject to the approval of the Secretary of Labor, will make and publish such rules and regulations as are necessary to the efficient operation of the legislation and will be required to submit each year to the Congress a full report of such administration.

As used in the bill, the term "state" means any state of the United States, the District of Columbia or any territory or possession of the United States.

Medical Legislation

MEDICAL BILLS IN CONGRESS

International Health Organization

Senator Pepper, Florida, for himself and Senator Wagner, New York, Senator Murray, Montana, Senator Capper, Kansas, Senator Ball, Minnesota, and Senator Smith, New Jersey, has introduced S. J. Res. 89 relating to the formation of an International Health Organization. After referring to the fact that the United Nations Conference at San Francisco adopted a recommendation to convene a conference to draw up the statutes of an International Health Organization, this joint resolution expresses the sentiment of Congress that there should be a speedy convening of such conference and the early formation of such an International Health Organization. If the joint resolution is adopted, the President, on behalf of the government of the United States, will be authorized to take immediate steps to hasten the convening of the conference and the formation of the organization.

Scientific Research

Senator Kilgore, West Virginia, for himself and Senator Johnson, Colorado, and Senator Pepper, Florida, proposes by S. 1297 to promote the progress of science and useful arts, to secure the national defense and to advance the national health and welfare. This bill would create a National Science Foundation to promote scientific research as an independent agency of the federal government.

Another bill relating to the same subject matter has been introduced by Senator Fulbright, Arkansas, S. 1248. This bill would create a Bureau of Scientific Research in the Department of Commerce.

The Byrd bill, S. 825, proposing to establish a Research Board for National Security, was favorably reported to the Senate, July 28.

Miscellaneous

A bill proposing an annual appropriation of not to exceed $100,000,000 to provide assistance to the states in establishing, maintaining, operating and expansion of school lunch programs, S. 962, has been reported to the Senate with recommendation that it pass.

Senator Langer, North Dakota, proposes by S. 1262 that the American Red Cross be authorized to award meat and fat ration tokens, shoe ration coupons and sugar ration coupons to persons donating blood to the American Red Cross for use by members of the armed forces.

Another bill introduced by Senator Langer, North Dakota, S. 1332, would provide maternity leave for government employees.

H. R. 3761, introduced by Representative Welch, California, proposes to amend in several respects the Longshoremen's and Harbor Workers' Compensation Act. One of the amendments would authorize an injured employee to select to treat him any physician authorized by the commission to render medical care to beneficiaries of the act. The commission would be authorized to establish such panels of qualified physicians, surgeons, specialists, consultants, "laboratory x-ray or other technicians," compensation medical bureaus and laboratories as may be necessary and would be authorized to establish schedules of fees to be charged by those rendering services to beneficiaries.

Official Notes

ELECTRICAL TRANSCRIPTIONS ON PUBLIC HEALTH

Effective August 14 the Bureau of Health Education offers an additional series of electrically transcribed radio programs for use by local medical societies or by local health agencies approved by such local societies.

The new series of health platters is entitled Guardians of Your Health. It consists of interviews and round table discussions featuring thirty-three public health authorities, including health officers of cities and states, laboratory directors, nurses and federal health officials. The theme of the series is medical and public health cooperation for the better health of the nation. The programs were prepared under the supervision of the Bureau of Health Education; scripts were written by Harriet Hester, who also interviewed the speakers; each program is summarized by Dr. W. W. Bauer, Director of the Bureau of Health Education. The titles and speakers are as follows:

1. Doctors Guard Your Health: Haven Emerson, M.D., New York; W. W. Bauer, M.D., Chicago.

2. Health in Your Town: M. R. French, M.D., Paw Paw, Mich.; Gertrude Cromwell, R.N., Des Moines, Iowa; Major Joel I. Connolly, Chicago.

3. The Healthy State: A. J. Chesley, M.D., St. Paul; Stanley Osborn, M.D., Hartford, Conn.

4. Guarding the Nation's Borders: Thomas Parran, M.D., Surgeon General, James P. Leake, M.D., C. C. Applewhite, M.D., U. S. Public Health Service.

5. Health in Our Hemisphere: John A. Ferrell, M.D., New York; Hugh S. Cumming, M.D., Pan American Sanitary Bureau.

6. Health in the Schools: Ruth Grout, Ph.D., Minneapolis; Charles C. Wilson, M.D., New York.

7. Sanitation—An Unfinished Job: H. G. Callison, M.D., South Carolina; F. C. Beelman, M.D., Kansas; Huntington Williams, M.D., Baltimore.

8. Guarding the Food Front: P. A. Dunbar, Ph.D., U. S. Food and Drug Administration; Willard H. Wright, M.D., U. S. Public Health Service.

9. Trained Public Health Workers: William P. Shepard, M.D., San Francisco; Agnes Fuller, R.N., New York.

10. The Public Health Laboratory: W. D. Stovall, M.D., Madison, Wis.

11. Controlling Contagious Diseases: Carl A. Wilzbach, M.D., Cincinnati; Thurman B. Rice, M.D., Indianapolis; Commander Dean F. Smiley, U. S. Navy.

12. Popular Health Crusades: Charles E. Lyght, M.D., Don W. Gudakunst, M.D., Walter F. Clarke, M.D., Philip Platt, C.P.H., New York.

13. Health Education: Donald Armstrong, M.D., New York; Thomas G. Hull, Ph.D., Chicago; Lester Taylor, M.D., Cleveland.

These platters are available on loan by application to the Bureau of Health Education. The series will be lent only as a whole and for broadcasting purposes only. There is no charge to the local group except payment of return shipping costs. All local broadcasting arrangements must be made by local groups. Scripts accompany platters; but material to be offered to listeners, if such offers are to be made, must be provided locally.

Washington Letter

(From a Special Correspondent)

Aug. 6, 1945.

War Department to Restaff Medical Units Deployed to Pacific

The War Department has announced that plans are being worked out to restaff all Army Medical Department units deployed through the United States to the Pacific with doctors who have not seen overseas service. It is also revealed that 1,000 medical officers have been requisitioned from Europe for return at the end of this month to relieve a shortage of doctors in army hospitals in this country. Recently Secretary Stimson informed Chairman Thomas of the Senate Military Affairs Committee that 7,000 doctors would be released during the next nine months for return to civilian practice. Senators have protested about the "leisurely attitude" of the Army toward the demobilization of doctors. Only 900 have been discharged since January 1. The Army explains that there will be an initial lag in the discharge of doctors over other officers because sick and wounded soldiers remain in hospitals long after the fighting is over. The War Department denies that the Army is overstaffed with medical officers by pointing out that personnel is slightly below the 45,000 ceiling set in September 1944, which was 5,000 below the ceiling set for the Army by the War Manpower Commission. The present ceiling will be cut by 7,000 in ensuing months and is said to be far under requirements set forth by Congress in its ratio of 6.5 doctors per thousand men.

Veterans Administration Medical Staff to Expand

Expansion of the entire Veterans Administration medical staff, professional and lay, is predicted in the next few years as more veterans of this war require hospitalization. Gen. Omar N. Bradley takes over the agency on August 15, heading one of the few federal agencies that will grow rather than shrink after the war. The administration had more than 63,000 at last report and it needs 2,000 nurses at once and 600 more doctors by the end of October. When the war ends, between 7,000 and 8,000 soldiers who are on detached service as orderlies, attendants, clerks and in other capacities will have to be replaced by civilians. Actuaries say that veterans' hospitals must be staffed to take care of 300,000 patients within twenty years. Considerable legislation, affecting veterans as well as reorganization of the agency, awaits recommendations of General Bradley when Congress returns from its recess early in October.

Proposed Control of Newly Discovered Synthetic Drugs

The Senate has passed and sent to the House legislation to allow the Treasury Narcotic Bureau to control the sale of numerous newly discovered synthetic drugs which are said to have the "dangerous, habit forming" qualities of morphine and cocaine. The present procedure requires that Congress pass a special law each time a new drug of this sort is placed on the market before the Treasury can issue regulations to control it. Chairman Walter F. George of the Senate Finance Committee said that the Treasury expected a number of new habit forming synthetic drugs to appear on the market any day. The proposed law would enable the Narcotic Bureau to act at once "before any great quantity" reaches the market, he said.

Further Requests for Better Artificial Limbs for Wounded Servicemen

Severe criticism of the artificial arms and legs which the government is supplying to wounded service men has been expressed editorially in Washington newspapers and in others throughout the country. The Washington *Daily News* said editorially "We don't know what's wrong or what specific steps should be taken to remedy the situation. We do know that some of the men who have given their arms and legs for this country feel deeply that they are not getting the proper appliances. This country, which has made efficient airplanes and rocket bombs, apparently hasn't produced workable artificial arms and legs." Newspaper comments further state that what the amputees want now is action, through coordinated research and effort, rather than a multiplicity of suggestions on what might be done. One newspaper said that "maybe we ought to have a Baruch report on artificial arms and legs. Not necessarily made by Mr. Baruch—perhaps by some leading doctors or medical institution, like the Mayo Clinic or Johns Hopkins." The government has appealed for new ideas on how to make better artificial arms and legs for wounded servicemen. An official of the National Inventors Council, a government agency set up to receive suggestions to help win the war, said "We need more ideas from the general public as well as inventors. The American people have always been inventive and ingenious. Maybe there is some plan not yet tried which would make better limbs." Research is now being conducted by the Army and Navy and in some private laboratories under auspices of the National Research Council. Several recently made suggestions are now being acted on.

Army Doctors in Pacific Find Replacements Delayed

Although the Army says it is relieving as speedily as possible its doctors who have been stationed for long periods in the Pacific, it is disclosed that delayed replacements from Europe have prolonged service of these medical officers. Some have been in the Pacific theater for as long as three years, enduring hardships and bad climate. The Surgeon General's Office estimates that it requires four to five months for a doctor to be shipped from Europe, furloughed in the United States and moved on to the Pacific on assignment relacement. A month is required after a doctor is relieved from permanent duty in Europe until he boards a home bound ship, and on reaching this country two weeks must elapse before he starts his thirty day furlough. Travel time then has to be figured for movement to a West Coast shipping center. Another thirty days is required crossing the Pacific to reach the ultimate destination. Then, before the Pacific Army doctor can leave for home, two weeks must be spent to acquaint the new man with the job.

Flood Interrupts Research on Tropical Disease

Medical research on tropical diseases was seriously disrupted when a "flash flood" drowned more than 200 experimental animals, including monkeys, dogs, cats, rats and mice, at the National Institute of Health near Bethesda, Md. Dr. R. E. Dyer, director of the institute, reported a loss in equipment and property of between $75,000 and $100,000. This, he said, was "nothing compared to the loss of strains of disease kept alive and under study in those animals. Some of them were flown here from China." Dr. Dyer said that records of much of the work were also lost. The disease under study is schistosomiasis, a tropical disease which attacks the liver. It was encountered by troops in the Southwest Pacific, infecting whole areas including the Philippines, the China Coast and Japan. The institute will have to send for more animals and start this special research all over again. The most serious loss is one of time.

U. S. War Casualties Total 1,061,648

The War Department reveals that war casualties for the week ended July 29 were 2,806, making a total of 1,061,648 since December 1941. Army losses are 197,676 killed, 570,766 wounded with 351,317 returned to duty, 34,734 missing and 117,741 prisoners of war, with 95,709 exchanged or returned to military control, making a total of 920,917. Navy losses are: Navy, 31,498 killed, 23,054 wounded, 10,547 missing, 2,038 prisoners, total 67,137; Marines, 19,385 killed, 50,465 wounded, 909 missing, 1,719 prisoners, total 72,478; Coast Guard, 808 killed, 213 wounded and 95 missing, total 1,116.

Civilians Clamor for Supplies of DDT

Since the revelation in the press that DDT, the magic insect killer, can be easily produced from nonpriority materials, drug stores throughout the country have been deluged with civilian requests for supplies. Already newspapers have printed news and feature stories describing in detail the formula and method of producing DDT. Official authority is awaited before large scale production for civilian use will be launched on a nationwide scale.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ALABAMA

Medical School Opens.—The Medical College of Alabama, Birmingham, opened officially June 4 with instruction of a junior class. On October 8 the School of Basic Medical Sciences on the University campus, where the first and second years are given, established in 1920, and its faculty will be absorbed into the new Medical College of Alabama. The School of Basic Sciences, direct successor in 1920 of the Medical College of Alabama at Mobile, organized in 1859, ceases to exist in October. The new Medical College of Alabama was established by action of the 1943 state legislature as a division of the University of Alabama. It was located in Birmingham in 1944 by vote of a special governor's commission. In 1945 it assumed title to Jefferson Hospital, Hillman Hospital, outpatient department, nurses home and all other city and county property of Jefferson County. In addition, the county and city gave to the university one block of property directly west, one half of which will be the site of a new health department building supported by state, county and city and to be affiliated with the Medical College of Alabama. Also two other blocks of adjacent property have been acquired by purchase by the university to serve as sites for other hospitals such as the Children's Hospital, the Crippled Children's Clinic and the Negro hospital, thus creating a four block medical center. In a fifth block south the university has purchased and remodeled apartment houses to provide living quarters for faculty and students. Under a ninety-nine year contract between the university and the county of Jefferson the Medical College of Alabama assumes responsibility for care of all indigent patients of county and city, maintenance of which is paid to the university on a per diem basis by the county. The 1943 appropr tion included one million dollars for the building and equipment of a new medical school, which will be erected as early as possible after the war and connected under one roof with the new Jefferson Hospital. Under its contract the medical college receives authority for the appointment of the entire staff, medical and otherwise, of the combined hospitals.

CALIFORNIA

Position Available as Chief of Tuberculosis.—The California State Personnel Board is requesting applications to fill the position as chief of the state bureau of tuberculosis. Applications must be filed by August 30, and an examination will be held September 13. California residence has been waived. Candidates who are successful in the examination must obtain a license to practice medicine in California before they will be considered eligible for appointment. Education must include graduation from an approved medical school, completion of one year internship in a recognized hospital and completion of one year's graduate course in a recognized school of public health as well as three years' experience in the practice of medicine, including one year of full time experience as resident or associate physician in a tuberculosis sanatorium or hospital with a capacity of at least 50 beds. The salary will be $480 a month. Additional information may be obtained from the California State Personnel Board, 1015 L Street, Sacramento 14.

LOUISIANA

Dr. Brown Resigns as Director of Tuberculosis Control.—Dr. Reuben Alec Brown, New Orleans, has resigned as director of the division of tuberculosis control of the Louisiana State Board of Health. Newspapers reported that Dr. Brown will enter private practice in Houston, Texas.

Veterans' Psychiatric Service.—A veterans' psychiatric service has been established at the Veterans' Information Center, New Orleans, under the sponsorship of the Louisiana Society for Mental Health. The service will be available for the benefit of mentally disturbed veterans who cannot afford the cost of the services of a private psychiatrist. Dr. Milton E. Kirkpatrick, New Orleans, is clinical director with Dr. Walker Thompson, New Orleans, and Major H. Halbert Leet, M. C., assisting him.

NEW YORK

Provisions for Mental Care.—Plans for a $120,000,000 mental hospital construction program have been filed with the state postwar planning commission by Dr. Frederick MacCurdy, New York City, commissioner of mental hygiene, in anticipation of a large increase in the number of postwar patients, according to the New York *Times*. The commission on July 20 had approved $45,000,000 of these proposals, and early approval is expected for the others. The patient population of the state hospitals increased from 38,294 in 1920 to 83,053 in 1942. There were 82,108 under care on June 1. The recent decline is ascribed to the fact that more than 1,000,000 residents of the state are in military service and many persons who obtained employment during the war might have become patients had they remained idle.

Cornell Adopts Compulsory Physical Training Program.—On July 21 Cornell University, Ithaca, announced the adoption of a permanent compulsory physical education training program "designed to make such training enjoyable rather than a chore and emphasizing games and particularly carry-over sports beneficial to health after graduation." The program, evolved after study of three years' experience in conditioning army and navy trainees, was recommended as a requirement for all first and second year civilian men by the department of physical education and athletics. Effective with the opening of the current term the program, which normally will affect 3,000 underclassmen, is tied in with a cooperative venture of the university's medical department to provide corrective exercises. Freshmen and sophomores will be required to devote three hours weekly to the program.

New York City

Tuberculosis Admission Bureau Has New Offices.—The Tuberculosis Admission Bureau of the New York City Department of Hospitals, formerly located at 125 Worth Street, now has its offices at 535 East Eightieth Street. Application cards should be sent to the new address. All tuberculosis applications of the greater city of New York clear through the bureau.

Personal.—The degree of doctor of science was conferred on Dr. Margaret Barclay Wilson, Washington, D. C., professor emeritus of physiology and hygiene, at the recent commencement of Hunter College.——Dr. Trigant Burrow was given a Jubilee diploma by Fordham University during its recent commencement. The diploma is conferred on those who have been graduated fifty years from Fordham.

Ledyard Fellowship Available.—The Society of the New York Hospital announces that the Lewis Cass Ledyard Jr. Fellowship is now available. Applications should be addressed before November 15 to the committee of the Lewis Cass Ledyard Jr. Fellowship, Society of the New York Hospital, 525 East 68th Street, New York 21. The fellowship was established in 1939 by Mrs. Ruth E. Ledyard in memory of her late husband, Lewis Cass Ledyard Jr., who was a governor of the New York Hospital. The income, amounting to approximately $4,000 annually, will be awarded to an investigator in the fields of medicine and surgery or in any closely related field. Of this amount $3,000 will be applied as a stipend and approximately $1,000 for supplies or expenses of the research. In making the award, preference will be given to younger applicants who are graduates in medicine and who have demonstrated fitness to carry on original research of high order.

Restrict Sale of Penicillin and Other Antibiotic Drugs.—On July 24 the New York City Board of Health added a new section to the sanitary code restricting the sale of preparations containing penicillin or other antibiotic drugs to persons presenting a written prescription of a physician, dentist, podiatrist or veterinarian except in the cases of preparations which the board of health at some future date may specifically exempt from the provisions of the section. The new ruling became effective on August 1. In announcing the change Dr. Ernest L. Stebbins, health commissioner, gave three principal reasons for the board's action: Undertreatment may alleviate the symptoms of the illness without curing the disease, which in turn may continue to be communicable to other persons and to produce damage to the infected person; "there is also accumulating evidence of possible importance of the development of penicillin fast strains in persons who are inadequately treated," and, finally, these antibiotic drugs have been recently developed and there has not been sufficient time to determine the possible toxic reactions.

Orthopedic Hospital Merges with Columbia-Presbyterian Center.—The New York Orthopaedic Dispensary and Hospital and the Presbyterian Hospital at the Columbia-Presbyterian Medical Center were consolidated on July 23. The new corporation will be known as the Presbyterian Hospital in the City of New York. The orthopedic hospital will remain at its present site, 420 East 59th Street, until the fifth floor of the Presbyterian Hospital at 622 West 168th Street, part of the medical center, has been cleared of 70 student nurses housed there temporarily. The facilities of the orthopedic hospital eventually will be transferred completely and the building will be sold, the New York *Times* stated. The 70 student nurses will live in two additions to Maxwell House, now being built as part of the medical center's eight million to nine million dollar expansion program, which, it is estimated, will take about two and one-half years to complete. The orthopedic hospital erected its present quarters in 1916, with additions in 1925 and 1931 providing its present capacity of 145 beds in private rooms and wards. The Columbia-Presbyterian Medical Center currently combines services and facilities of the Presbyterian Hospital, Sloane Hospital for Women, Vanderbilt Clinic, Babies Hospital, Neurological Institute, Harkness Pavilion, Institute of Ophthalmology, J. Bentley Squier Urological Clinic, School of Nursing and the teaching facilities of the College of Physicians and Surgeons of Columbia University. Announcement was made also that a new 75 bed convalescent hospital for orthopedic patients would be built on property in King Street, Port Chester, N. Y., belonging to the orthopedic hospital. The Mary Harkness Home for Convalescent Care is on the 80 acre tract in Port Chester.

PENNSYLVANIA

Medical Club Observes Twenty-Fifth Anniversary.—The Bethlehem Medical Club celebrated its twenty-fifth anniversary in Bethlehem on June 7. Dr. Arno R. Zack, president, was toastmaster. Among the speakers were Dr. William L. Estes Jr., first president of the club, who recalled the initial steps taken by the Bethlehem physicians to organize a club in 1910 to "eliminate professional jealousy and to promote good fellowship."

Philadelphia

New Professor of Pathology.—Dr. Mollie A. Geiss has been appointed professor of pathology at the Woman's Medical College of Pennsylvania to succeed Dr. Helen Ingleby, who resigned in June to accept the position of pathologist at the Jewish Hospital (THE JOURNAL, July 7, p. 743). Dr. Geiss has been on the faculty of the college since 1923 and associate professor of pathology since 1932.

Temple Commencement Activities.—On June 21, during the commencement exercises of the Temple University School of Medicine, the degree of doctor of medicine was conferred on 127 young men and women coming from twenty different states, also Puerto Rico and the Hawaiian Islands. Eighty of the graduates were commissioned first lieutenants in the medical corps of the Army of the United States and 32 as lieutenants, junior grade, in the U. S. Naval Reserve. The commencement address was delivered by Charles F. Kettering, D.Sc., vice president and head of the research department of General Motors. Robert Silvercruys, Belgian ambassador to the United States, also delivered an address. Honorary degrees were conferred on both of these speakers. Eight physicians completed three years of postgraduate work and were awarded the degree of master of science in the specialty studied. Henning W. Prentis Jr., president of the Armstrong Cork Company, Lancaster, Pa., gave the principal address at the 121st annual commencement of Jefferson Medical College of Philadelphia, June 22. His subject was "The R's of Professional Education." He was given the honorary degree of doctor of laws. The present graduating class of 152 members brings the total number of graduates up to 17,507 during the 121 years of existence. The members of the graduating class were registered from twenty-one different states and two insular possessions. Ninety-five members of the graduating class received first lieutenant commissions in the medical corps, Army of the United States. Four members received first lieutenant, medical reserve corps, commissions. Presentation of commissions was by Lieut. Col. Frederick Hubbell Mills, M. C. These students received commissions after completing the requirements of the Army Specialized Training Program. Forty-one members of the graduating class received lieutenant, junior grade, commissions in the U. S. Naval Reserve. The commissions were presented by Capt. Lemuel M. Stevens, U. S. Navy, retired. Nineteen members of this group went on active duty as U. S. Naval interns. The presentation by the graduating class of 1945 of a portrait of Dr. Edward L. Bauer, professor of diseases of the child, was reported in THE JOURNAL, June 9, page 454.

GENERAL

Kansas Accident Report.—The 1945 edition of the "Kansas Accidental Death Report," which has been compiled annually for a little more than a decade, established trends and patterns in the occurrence of accidents. The state of Kansas, being industrial, agricultural, urban and rural, furnishes all kinds of situations in which accidents can occur.

Lawrence Linck Named Executive Director of Crippled Children Society.—Lawrence J. Linck, Chicago, has resigned as director of the Illinois division of services for crippled children to become executive director of the National Society for Crippled Children. Simultaneous with this report was one announcing the removal of the executive offices of the society from Elyria, Ohio, to Chicago. Mr. Linck will take over his new work September 1, at which time the new quarters are expected to be opened.

Research Fund Named for Sir Alexander Fleming.—The University of Pennsylvania on July 25 was selected to administer an $80,000 research fund established by American manufacturers of penicillin for Sir Alexander Fleming, discoverer of the drug. According to the New York *Times* the selection was a tribute to the role played in the development of the drug by Dr. Alfred N. Richards, vice president of the university in charge of medical affairs, who is credited with starting the program of producing the drug commercially. Under the terms of the trust, Sir Alexander has the widest latitude in administration of the money for scientific purposes. The results of the research will be free to any one. The work will be carried on by Sir Alexander at St. Mary's Hospital Medical School, University of London.

Meetings Canceled.—The council of the American Pharmaceutical Association has voted to postpone indefinitely the meeting of the council originally scheduled to be held in Chicago in September.——The executive council of the Association of Military Surgeons of the United States has voted to cancel the annual meeting, which was to have been held in Detroit October 24-27. The council further voted to retain in office the present officers of the association and to hold the 1946 meeting in Detroit.——The convention of the Aero Medical Association of the United States scheduled for September 24-26 at the Palmer House, Chicago, has been postponed.——The fifth International Assembly of the International College of Surgeons, which was announced for September 10-12 in Lima, Peru, has been postponed. The assembly will be held as soon as travel facilities become available. Dr. Max Thorek, 850 West Irving Park Road, Chicago 13, is international general secretary of the International College of Surgeons.

Prevalence of Poliomyelitis.—Reports of cases of poliomyelitis for the week ended July 28 have been received from the division of public health methods, U. S. Public Health Service, as follows:

Division and State	Week Ended 7/28, 1945	Week Ended 7/29, 1944	Division and State	Week Ended 7/28, 1945	Week Ended 7/29, 1944
New England			North Carolina	2	57
Maine	6	..	South Carolina	7	2
New Hampshire	2	1	Georgia	4	8
Vermont	2	..	Florida	6	3
Massachusetts	13	8	East South Central		
Rhode Island	..	..	Kentucky	3	79
Connecticut	11	3	Tennessee	29	10
North Atlantic			Alabama	9	13
New York	72	237	Mississippi	1	1
New Jersey	32	3	West South Central		
Pennsylvania	16	64	Arkansas	..	..
East North Central			Louisiana	6	11
Ohio	14	40	Oklahoma	12	3
Indiana	2	20	Texas	40	8
Illinois	3	15	Mountain		
Michigan	8	30	Montana	1	1
Wisconsin	..	6	Idaho	..	..
West North Central			Wyoming	2	..
Minnesota	..	8	Colorado	1	..
Iowa	2	4	New Mexico	..	..
Missouri	2	..	Arizona	1	1
North Dakota	..	..	Utah	11	2
South Dakota	..	..	Nevada	..	..
Nebraska	..	1	Pacific		
Kansas	4	9	Washington	9	1
South Atlantic			Oregon	1	12
Delaware	..	1	California	21	13
Maryland	8	17	Total	391	740
District of Columbia	5	4	First 30 weeks:		
Virginia	22	39	1945 and 1944	2,439	3,060
West Virginia	1	5	Median, 1940-1944	1,526	

Advisory Council for Insurance Research Fund.—An advisory council of eight members has been appointed for the life insurance medical research fund including the following:

Dr. Francis G. Blake, dean, Yale University School of Medicine, New Haven, Conn.
Dr. Ernest W. Goodpasture, dean, Vanderbilt University School of Medicine, Nashville, Tenn.
Albert Baird Hastings, Ph.D., Hamilton Kuhn professor of biochemistry, Harvard Medical School, Boston.
Dr. Eugene M. Landis, George Higginson professor of physiology, Harvard Medical School.
Dr. Robert F. Loeb, professor of medicine, Columbia University College of Physicians and Surgeons, New York.
Dr. Cyril N. H. Long, Sterling professor of physiologic chemistry, Yale University School of Medicine.
Dr. Seeley G. Mudd, professor of experimental medicine, University of Southern California School of Medicine, Los Angeles.
Dr. Cecil J. Watson, professor of medicine, University of Minnesota Medical School, Minneapolis.

The creation of the research fund was sponsored by the American Life Convention and the Life Insurance Association of America (THE JOURNAL, June 23, p. 606). A newly appointed council was nominated by a committee of four physicians including Drs. Alan Gregg, director of medical sciences, Rockefeller Foundation, New York; Alfred N. Richards, vice president in charge of medical affairs, University of Pennsylvania School of Medicine, Philadelphia; Lewis H. Weed, director, school of medicine, Johns Hopkins University, Baltimore, and Dr. Blake.

CANADA

National Immunization Week.—September 30-October 6 has been designated National Immunization Week, according to the Health League of Canada, which is sponsoring the observance in cooperation with health departments. The week is devoted to intensifying efforts to promote immunization against diphtheria, smallpox, whooping cough and scarlet fever.

Annual Meeting of Health League.—The twenty-sixth annual meeting of the Health League of Canada, formerly known as the Canadian Social Hygiene Council, will be held at the King Edward Hotel, Toronto, September 26-28. The theme of the meeting will be disease prevention, with separate sessions to discuss immunization, industrial health, nutrition, pasteurization and venereal diseases.

Degree Course in Physical Education.—McGill University, Montreal, has established a degree course in physical education, the first class to start in September. The course will be of four years' duration following junior matriculation or three years following senior matriculation or its equivalent. Open to both men and women students, it will lead to a degree of bachelor of science in physical education. The curriculum will include courses in English, physics, chemistry, zoology, anatomy, physiology, psychology, sociology, education, bacteriology, organization and administration, history, development and present day requirements in mental health, preventive medicine, nutrition and the technical application of physical medicine. Progressively arranged throughout the four years will be the technical and professional material involving basic technics in neuromuscular activity, principles of physical education, analysis and practice of activity, methods and analysis of teaching, curriculum content and planning, and practice teaching. The school of physical education at McGill, said to be the oldest of its kind in Canada, was established in 1912. The new program will be the first degree course offered by the school, which is an integral part of the faculty of medicine.

FOREIGN

Pasteur Institute Receives Grant for Penicillin.—The French government has made a grant of 10,000,000 francs to the Pasteur Institute, Paris, to enable it to develop research into the preparation of penicillin, it is reported.

Memorial Service for Dr. Thierry de Martel.—Impressive religious services were held June 14 at Neuilly-sur-Seine in memory of Dr. Thierry de Martel, formerly chief surgeon at the American Hospital of Paris. Dr. de Martel had reached his sixty-fifth birthday in June 1940, when the Germans entered Paris. On the night of June 13-14 he took his own life, thus obviating practically certain imprisonment and compulsion to work for the Germans against his own countrymen.

Personal.—Major Greenwood, D.Sc., has retired as professor of epidemiology and vital statistics at the University of London School of Hygiene. Because of a change in the distribution of teaching and the steady increase in the volume of research work and teaching within the field of medical statistics, the title of the chair has been altered to that of medical statistics and A. Bradford Hill, since 1933 leader in medical statistics in the university, has been appointed to succeed Dr. Greenwood, who has been given the title of professor emeritus in epidemiology and vital statistics.

Government Services

Care of Children in Liberated Countries

Support of the National Commission on Children in Wartime to the policies of the United Nations Relief and Rehabilitation Administration in the care of children in the liberated countries was expressed in a statement prepared by a committee of the commission and released recently. In view of the frightful things that have happened and are happening to children and the need for prompt action in identifying children and restoring them wherever possible to their families, the statement urged that the policies be developed immediately by the highest army authorities and UNRRA in regard to the services to be rendered by the latter in dealing with displaced children in territories under military control. In addition to expressing concern as to the fate of thousands of homeless children, the committee in its conference with Herbert Lehman, director general of the UNRRA, June 12, stressed the need for arousing the people of this country to the fact that children in Europe are starving or near starvation because they do not have the protective foods, particularly meat and milk, to which this country must be looked as the main source of supply. The committee included Mr. Leonard W. Mayo, Cleveland, head of the committee of the National Commission on Children in Wartime and president of the Child Welfare League of America; Katharine F. Lenroot, Washington, D. C., chief of the Children's Bureau, U. S. Department of Labor; J. Milton Patterson, Chicago, American Public Welfare Association; Maxwell Hahn, New York, Field Foundation, and Dr. Leona Baumgartner, New York, American Public Health Association.

Meeting of the National Advisory Health Council

At a meeting of the National Advisory Health Council at the headquarters of the U. S. Public Health Service, Bethesda, Md., June 19-20, to discuss current and future activities of the several bureaus of the public health service, recommendations were made that:

A committee of the council be appointed to act with designated officers of the service in the development of a program of clinical research in the Public Health Service.

The Public Health Service strengthen its control of the interstate spread of disease through consultant services to public health laboratories and through maintenance of a $1,000,000 emergency fund to be used in epidemics and disasters.

The Public Health Service undertake demonstrations in selected communities of generalized public health nursing programs, including bedside care.

The Public Health Service establish a training program for its own personnel, which would include orientation, work experience, observation, in-service training, and opportunities for state and local personnel to participate.

The program of grants-in-aid and technical services to the states in the field of industrial hygiene be expanded.

The Public Health Service seek appropriations for grants-in-aid for general research to be allotted to qualified institutions and individuals.

When the federal government undertakes grant-in-aid programs related to public health and sanitation, the Public Health Service be empowered to conduct investigations for determination of the nature and extent of the problems involved and to approve the allocation of funds, functional effectiveness and placement of plants, installations and constructions required of such programs.

The council also recommended the approval of a grant in aid of $92,000 to the University of Utah for research on muscular dystrophy, which, according to an announcement, is the first grant-in-aid for general research projects to be made under the provisions of the public health service act of 1944 (P. L. 410). This is the law that authorized the council, which had been serving in only an advisory capacity, to have the legal responsibility to:

. . . advise, consult with and make recommendations to the Surgeon General on matters relating to health activities and functions of the service; and to serve in other capacities as requested.

Recommend research projects for grants-in-aid in scientific fields other than cancer research, and recommend other procedures for the advancement of scientific research.

Recommend the adoption of regulations by the service with respect to interstate quarantine for the prevention of communicable diseases, including regulations for the apprehension, examination and detention of persons who are spreading disease.

The council will hold regular meetings twice a year, special meetings to be called as needed. Members of the council are to serve as chairmen of special committees dealing with specific subjects.

Foreign Letters

LONDON

(From Our Regular Correspondent)

July 21, 1945.

The Slowness of Medical Demobilization: Government Criticized by the British Medical Association

For some reason which the government will not explain, demobilization of the fighting services is very slow. In the case of medical service great dissatisfaction has been expressed by the British Medical Association. At a meeting held at the headquarters of the association Dr. Guy Dain, chairman of the council of the association, who presided, explained that the association could not find out which groups of doctors were likely to be demobilized. The position with regard to the civilian population was very difficult. Doctors were very badly needed and the profession had been driven to great lengths to meet that need. Doctors were not able to get back to their practices, and the association was getting many letters of protest from men who were serving but so far had not been able to get any satisfaction. The profession had carried on at home with the ratio of 1 doctor to 3,000 civilians in urban areas and 1 to 2,400 in rural areas, whereas in the fighting forces there was on an average 1 doctor to every 350 men.

Dr. Charles Hill, secretary of the British Medical Association, said that unless at least 5,000 doctors were released for work among the civilian population next winter a grave situation might arise in the event of an epidemic. In a letter to the *Times* he pointed out that approximately one third of the doctors in the country are serving with the forces. The Central Medical War Committee of the association suggested the continuance of recruitment after the end of the German war in order to facilitate demobilization, and the government accepted this. Although recruitment is proceeding, the committee has not been informed of the quota of doctors to be supplied for 1945. Accordingly it does not know the extent to which, if at all, the recruitment will find expression in accelerated release. In spite of repeated requests the committee has not been informed of any time table for demobilization apart from certain groups. Until a long term program is announced, the intense dissatisfaction which now exists will continue. The government has decided, against the protest of the committee, not to continue to recruit medical women. This decision will hamper recruitment and so delay demobilization.

Great Success of Medical Measures in the Burma Campaign

The campaign in the malarious jungles of Burma has been a serious problem for the army medical service. In the early days sickness, largely due to malaria, was as high as 300 per cent annually. Whole units were incapacitated at a time. But, thanks to new methods vigorously applied, the rate has been reduced to only 4 per cent. Only two years ago 70 per cent of all army sickness was due to malaria. Last year this rate fell to 36 per cent and in the first four months of the present year to 27 per cent. The malaria rate has been reduced to 17 per cent of what it was at the corresponding time last year.

This astonishing improvement is due to the thoroughness of the antimalaria measures. Close behind the advancing troops both the ground and the air forces send out men to survey malarious tracts of country, select camp sites and plan the work of the malaria control units. Camp areas are sprayed with the insecticide DDT. Trickling jungle streams, the seepage of swamps, are canalized or attacked with DDT, for these are the breeding places of Anopheles minimus, the cause of the high malarial rate in Assam. Brackish swamps and lagoons near the sea are the breeding places of another variety of mosquito, Anopheles sundaicus, which infects the Arakan coast. These places are oiled or drained by deep channels into tidal streams. Last year three new measures were adopted: the administration of mepacrine to the troops; the introduction of DDT, which is not only sprayed in tents and buildings but over malarious tracts of country by low flying aircraft, and the use by forward troops of fish net veils soaked in "scat," the American repellent dimethyl phthalate. Under military discipline every soldier takes daily a tablet of mepacrine and wears long trousers and buttoned sleeves to reduce the risk of mosquito bites.

Another advance is the sending of supplies by air. When the medical officer commanding an advanced unit requires anything, he radios to the base and within a few hours is supplied by parachute. Even blankets and stretchers are dropped by air, and surplus supplies are returned with the wounded. Under this system the amount of stock that need be kept on hand by the unit is much reduced and the advantage is gained that the unit can travel light.

Great Development of Rehabilitation Treatment

As reported previously in THE JOURNAL, rehabilitation has received much increased attention as a result of war injuries. The present position is summarized in an address by the minister of health, Mr. Willink, to representatives of the British Council for Rehabilitation. In the Emergency Medical Service (established during the war mainly for the treatment of civilian casualties due to German air raids) more than 11,000 patients are taking daily courses of remedial exercises in their beds. In addition 20,000 are attending hospitals for special exercises and remedial games. Of these 31,000 persons receiving rehabilitation, 15,000 are taking part in some form of occupational therapy. Since the Ministry of Health made a special survey with the object of extending these facilities, the number of hospitals providing rehabilitation for their patients has increased from 150 to 300. The great majority of the sick and wounded from the fighting services are receiving their medical rehabilitation in the hospitals of the Emergency Medical Service. More than 250 doctors have been given special training, and for hospitals handicapped by lack of accommodation the ministry has provided thirty-four prefabricated buildings. Conferences have been held throughout the country for leaders of industry, personnel managers, welfare officers and industrial medical officers, to explain the whole process of rehabilitation and the part which industry has to play in the resettlement of patients.

The minister of health added that there is no intention to relax this campaign. Wartime progress must not be lost in peacetime. The success of rehabilitation methods would lead to increased demand which hospitals throughout the country were already getting ready to meet. The Ministry of Health would retain its Rehabilitation Department and was fully prepared to continue to encourage and assist the development of these facilities as an integral part of the health services. The British Council for Rehabilitation could perform a most useful work in bringing together the medical and industrial points of view.

Science Under the Nazis in Denmark and Norway

Prof. A. V. Hill, secretary of the Royal Society, has returned from a visit to Norway and Denmark to present to the academies of the two countries the greetings of the society and copies of all that it has published since 1940. He reports that science has not suffered under the Nazis in Denmark as badly as in most countries. Until the autumn of 1943 they were on their best behavior, but then the Gestapo became active and students ceased to attend the colleges. Professor Rehberg, zoologist, was brutally mishandled for lack of cooperation and, with many other scientists, was imprisoned. The chief scientific need is books and journals and English textbooks for students. But so

quickly have the Danes reestablished themselves that they are contemplating an expedition for marine biologic investigation off the west coast of Africa.

Norway has suffered more than Denmark. The president of the academy, Professor Bull, was three years in a concentration camp. The scientific laboratories were stripped of equipment, and scientific work suffered and the Norwegians have great difficulties in getting their courses started again. Medicine attained a high standard in Norway before the war. The Danes are taking a large number of Norwegian medical students, and Norway is anxious that some of her best postgraduate students should study over there. In both countries the most friendly relations exist with Britain, and English bids fair to become a second language. Both desire to use our books and scientific instruments in place of those formerly imported from Germany.

Visit of Brazilian Plastic Surgeon

Dr. David Adler, consulting plastic surgeon to the Air Force Hospital, Rio de Janeiro, is in this country on a six months visit, arranged by the British council. During his visit he will work with Sir Harold Gillies, the leading British plastic surgeon.

BRAZIL

(From Our Regular Correspondent)

Rio de Janeiro, June 30, 1945.

Penicillin in the Treatment of Frambesia

Dr. A. Marques da Cunha and Dr. A. Area Leão, at the Oswaldo Cruz Institute, have been conducting extensive studies and experimentation for several months on the therapeutic effects of penicillin in some important tropical diseases. One series of studies relates to frambesia, or yaws, a disease in which the extensive skin lesions and the abundance of treponemes permit objective evaluation of the results of treatment. The first experiments were performed with barium penicillin solution prepared at the institute. Seven patients treated with penicillin alone were clinically and microscopically cured in twelve to forty-four days. The penicillin was injected at intervals of four to six hours, 200 Oxford units being used each time. The total dose per patient varied from 9,600 to 52,000 units. In spite of the frequency and the number of injections, no toxic effects were noted. The patients were maintained during six months under weekly immunologic control.

The second group of experiments involved 5 patients treated with dried sodium penicillin of American make. The same dose of 200 units was used, adding up a total which varied from 24,000 to 54,000 units for each patient. The healing of the skin lesions and the disappearance of the subjective symptoms were obtained as in the first series of patients. The immunologic cure in all the cases of the two series did not immediately accompany the clinical cure: it took a few months to develop negative Wassermann reactions in all the 12 cases.

Revision of the Pan American Sanitary Code

The tenth Pan American Conference of National Directors of Health, held in Washington in 1944, decided to amend the present Pan American Sanitary Code, adopted twenty-five years ago by the nations of the Western Hemisphere. In fact, the present code in many points is not in accordance with the advancements of the medical sciences and is quite inadequate in some others to meet the conditions created by the rapid development of air transportation. Furthermore, some new subjects, in addition to the control of transmissible diseases, need to be included in the code as the sanitary activity has been expanded to comprehend a few modern problems. According to that decision Dr. Hugh S. Cumming, director of the Pan American Sanitary Bureau, appointed Dr. J. de Barros Barreto, director general of the National Department of Health of Brazil, Dr. Solon Nunez, secretary general of health of Costa Rica, Dr. Rafael Schiaffino, director of the department of health of Uruguay, and Dr. Garza Brito, professor at the School of Public Health of Mexico, to prepare a draft of a new code, to be presented to the twelfth Pan American Sanitary Conference, to be held in Caracas, Venezuela, in 1946. The committee is now working at Rio de Janeiro under the chairmanship of Dr. Barros Barreto.

Experimental Infection with Leishmaniasis Americana

The experimental infection with leishmaniasis americana is a subject not yet sufficiently studied. Dr. A. Marques da Cunha of the Oswaldo Cruz Institute has just published an interesting paper on an experimental study in which he succeeded in infecting the rhesus monkey with the agent of the disease (Leishmania brasiliensis), causing the production of mucous lesions similar to the ones described in man. The causative agent of leishmaniasis americana should not be confused with the agent of American kala-azar, or visceral leishmaniasis, i. e. Leishmania chagasi. The inoculations were made intradermally about the superciliary arches or into the skin of the nose. The incubation period ranged from one to two months. The course of the infection varied according to whether the lesions were limited to the skin or also invaded the mucous membranes. In the former the infection lasted from three to eight months and always terminated in spontaneous cure. When the lesions were also present in the mucous membranes they tended to persist and evolve, while the skin lesions observed in the same animal became regressive and tended to healing and cure. Dogs also were inoculated, with positive results, the incubation period being about two months and the skin lesions tending always to terminate by cure. Other tropical monkey-like animals, such as Dasyprocta agouti, when inoculated never showed the infection. One rhesus monkey which recovered from an infection by L. brasiliensis could not be infected when inoculated with another strain of the same parasite. The extent of the lesions of the mucous membranes in experimental infections of rhesus monkeys by Leishmania brasiliensis, a fact not yet observed with Leishmania tropica, constitutes a strong argument in favor of the independence of the two species.

Marriages

Donald Ewing Tinkess, Greenwich, Conn., to Mrs. Clyde Manson Trotter of Chattanooga, Tenn., in Columbia, S. C., June 16.

Aníbal Roberto Valle, Charlottesville, Va., to Miss Rose Mary Keupper of Gillespie, Ill., in Washington, D. C., June 25.

Richard Phillips Bell, Staunton, Va., to Lieut. Hilda Steele Franklin, A. N. C., of Fieldale, May 26.

Malcolm C. Todd, Lawrenceville., Ill., to Miss Ruth Holle Schlake of Chicago in London, England, June 12.

Francis Michael Smith Jr., Vicksburg, Miss., to Miss Betty Thibaut of Donaldsonville, La., in June.

James Leonidas Camp III, Franklin, Va., to Miss Jane Elizabeth Geuting in Philadelphia in May.

Frederick William Wood Jr. to Miss Patricia M. Wright, both of Garden City, N. Y., June 15.

Robert Loftus Brereton, Kirkwood, Mo., to Miss Ann Van Dyke of St. Louis, June 23.

William Parks Blackmon, Atlanta, to Miss Dorothy Mae Ware of Mayo, Fla., June 21.

Gustav Julius Beck to Miss Rita Levitiss, both of Gloversville, N. Y., May 12.

Orville W. Winters to Miss Ruth Mae Weber, both of Cincinnati, July 28.

George C. Truman, Mesa, Ariz., to Lieut. Dorothy Hinson recently.

Lynn McIver to Miss Elva Bryan, both of Sanford, N. C., June 5.

Deaths

James Bertram Overton, Talmage, Calif.; Washington University School of Medicine, St. Louis, 1931; began active duty as a captain in the medical corps, Army of the United States, on Nov. 13, 1942; assigned to chief neuropsychiatric service at Stockton; transferred to several other fields, serving also at Denver; relieved from active duty because of physical disqualification on June 25, 1944; honorably discharged Dec. 21, 1944; at one time associated with the U. S. Public Health Service Reserve; interned at the State of Wisconsin General Hospital in Madison and Johns Hopkins Hospital in Baltimore; interned at the Evansville (Ind.) State Hospital, where he also served a residency; served a residency at the Arizona State Hospital, Phoenix, New Mexico State Hospital, Las Vegas, Weston State Hospital, Weston, W. Va., Utah State Hospital, Provo, and at the Mendocino State Hospital, where he had been a member of the regular staff; died in Ukiah March 28, aged 40, of cerebral hemorrhage.

William Hamilton Jefferys, Haverford, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1898; formerly a medical missionary in China, where he served for many years as professor of surgery, lecturer on tropical diseases and dean at St. John's University and associated with St. Luke's and St. Elizabeth's hospitals in Shanghai; fellow of the College of Physicians of Philadelphia; past president of the American Association of China; honorary fellow of the China Medical Society; chairman, instruction committee, and vice president of the Pennsylvania Institute for Instruction of the Blind in Philadelphia for many years; served as executive superintendent of the Home for Consumptives in Chestnut Hill; retired superintendent of the Philadelphia Protestant Episcopal City Mission; formerly editor of the *China Medical Journal*; author of several books and articles on Christian mysticism; died in Philadelphia May 14, aged 73.

Orley Mason Vaughan Jr., Covert, Mich.; Northwestern University Medical School, Chicago, 1911; chairman of the board of the Tri-County Telephone Company, which he organized in 1924, serving as its president in 1940; instrumental in organizing the Michigan Independent Telephone Association; a director of the United States Independent Telephone Association; past president of the board of education of Covert; instrumental in creating the Covert Consolidated school district, of which he was also president; served as chairman of the county poor commission; died in Fort Lauderdale, Fla., April 23, aged 60, of cerebral hemorrhage.

John Mark O'Farrell, Houston, Texas; Memphis (Tenn.) Hospital Medical College, 1891; member of the American Medical Association and of its House of Delegates in 1920; honorary member of the State Medical Association of Texas; past president of the South Texas Medical Association; served during World War I; lieutenant colonel, medical reserve corps, U. S. Army, not on active duty; a member of the first state board of health; served on the staffs of the Memorial, Methodist and Jefferson Davis hospitals; for many years surgeon for the Santa Fe Railroad; died May 23, aged 79.

Harvey Arbuckle, Boonton, N. J.; College of Physicians and Surgeons, Baltimore, 1904; died May 13, aged 71, of congestive heart disease and pernicious anemia.

LIEUT. ANTHONY GUS KERASOTES
(MC), U.S.N.R., 1912-1944

LIEUT. (JG) JOHN F. KINCAID JR.
(MC), U.S.N.R., 1917-1945

LIEUT. COMDR. DANIEL J. MCCARTHY
(MC), U.S.N.R., 1908-1945

KILLED IN ACTION

Anthony Gus Kerasotes, Springfield, Ill.; St. Louis University School of Medicine, 1940; member of the American Medical Association; interned at St. Mary's Group of Hospitals in St. Louis; entered the medical corps of the U. S. Naval Reserve as a lieutenant (jg) on Sept. 10, 1942; received training at Parris Island, N. C., and served as medical officer at Savannah, Ga., naval base; participated in the invasions of North Africa and Sicily and the landings in Italy; served on board the U. S. S. *Leary* when the vessel was torpedoed in the Atlantic area while engaged in an antisubmarine patrol; promoted to lieutenant; reported missing in action as of Dec. 24, 1943; presumptive date of death Dec. 25, 1944, aged 32.

John Franklin Kincaid Jr., Leesburg, Va.; Duke University School of Medicine, Durham, N. C., 1942; diplomate of the National Board of Medical Examiners; interned at the Johns Hopkins Hospital in Baltimore; began active duty as a lieutenant (jg) in the medical corps of the U. S. Naval Reserve on July 10, 1943; died in the Asiatic area April 12, aged 27, of blast concussion.

Daniel Joseph McCarthy, Savannah, Ga.; St. Louis University School of Medicine, 1935; member of the American Medical Association; interned at St. Louis City Hospital; served as assistant resident surgeon at St. Joseph Hospital; entered the medical corps of the U. S. Naval Reserve as a lieutenant (jg) on Oct. 2, 1940; began active duty in the same grade on July 28, 1941, assigned to Charleston, S. C.; later promoted to lieutenant and lieutenant commander; died in the Pacific area February 22, aged 36, of fragment wound of the upper extremities.

Henry George Blanchard, Fairmont, Minn.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1897; member of the American Medical Association; died in the Community Hospital April 13, aged 76, of chronic myocarditis and arteriosclerosis.

Charles H. Burton, Iva, S. C.; University of Georgia School of Medicine, Augusta, 1903; formerly mayor of Iva; died May 2, aged 68, of coronary thrombosis.

George Harold Carpenter, Marion, Ohio; Toledo Medical College, 1912; died April 9, aged 61, of pneumonia.

Henry Clinton Cooney ✠ Princeton, Minn.; College of Physicians and Surgeons of Chicago, 1887; fellow of the American College of Surgeons; served as president of the Northern Minnesota Medical Association and the East Central Minnesota Medical Society; until March 1944 local health officer; for many years local surgeon for the Great Northern Railway; owner and medical director of the Northwestern Hospital; died April 1, aged 81, of cardiac decompensation.

Charles Aaron Hull, Omaha; Denver College of Medicine, 1893; formerly assistant professor of surgery at the University of Nebraska College of Medicine; fellow of the American College of Surgeons; at one time on the staff of the Immanuel Hospital; served during World War I; died May 8, aged 75, of bronchopneumonia and cerebral hemorrhage.

James Riley Kinney, Fort Valley, Ga.; Southern Medical College, Atlanta, 1889; at one time mayor of Fort Valley; died May 9, aged 81, of chronic myocarditis and arteriosclerosis.

Frederick Willer Meyer ✠ Capiz, P. I.; Yale University School of Medicine, New Haven, Conn., 1919; fellow of the American College of Surgeons; a member of the House of Delegates of the American Medical Association, 1937-1938; a missionary of the American Baptist Foreign Mission Society; director and chief surgeon, Emmanuel Hospital; died on the Island of Panay Dec. 20, 1943, aged 51, while in the custody of the Japanese.

Davis Strom Porter, Andrews, S. C.; Atlanta College of Physicians and Surgeons, 1910; served as mayor and councilman; for many years physician and surgeon for the Atlantic Coast Lumber Corporation and the Seaboard Railroad; died in a Florence hospital March 31, aged 62, of nephritis and cardiac decompensation.

Otto William Schwalb, Fort Lauderdale, Fla.; University of Georgia Medical Department, Augusta, 1928; member of the American Medical Association; served as secretary of the Georgia Medical Society; director of the Broward County Health Department; member of the tuberculosis board of Broward County; formerly city physician of Savannah, Ga.; died April 17, aged 42, of coronary thrombosis.

Capt. Aaron Emil Oswald
M. C., A. U. S., 1914-1945

Capt. Leroy William Yolton,
M. C., A. U. S., 1900-1945

Lieut. Charles W. Pfeiffer
M. C., A. U. S., 1918-1944

KILLED IN ACTION

Aaron Emil Oswald, Casper, Wyo.; College of Medical Evangelists, Los Angeles, 1941; interned at St. Luke's Hospital in Denver; served as assistant chief resident physician at Kern General Hospital in Bakersfield; commissioned a first lieutenant in the medical corps, Army of the United States, on May 27, 1942; later promoted to captain; bomber squadron flight surgeon; during the nearly two years that he was overseas he had been twice decorated for valor, the first for "meritorious achievement" while participating in aerial flights in the Southwest Pacific area from Jan. 5 to Oct. 3, 1944, and the second decoration, the Soldiers' Medal, was awarded to him in August 1944 for saving a gunner from burning plane wreckage; died February 24, aged 30, from a bomb-load explosion that followed his rescue of a pilot trapped in a burning plane on Morotai Island in the Pacific.

Leroy William Yolton ✠ Bloomington, Ill.; Rush Medical College, Chicago, 1931; interned at St. Luke's Hospital in Chicago, where he served a residency; began active duty as a captain in the medical corps, Army of the United States, on Sept. 3, 1942; killed in action in Luzon, P. I., February 3, aged 44.

Charles William Pfeiffer, Racine, Wis.; University of Chicago School of Medicine, 1942; interned at the Augustana Hospital in Chicago; at the age of 21 was commissioned a second lieutenant in the Field Artillery, since he was an R. O. T. C. member after graduating from Culver; on receiving his medical degree was transferred to the Medical Officers Reserve Corps with the rank of first lieutenant; began active duty on Dec. 30, 1943 as a first lieutenant in the medical corps, Army of the United States, and was assigned to the O'Reilly General Hospital in Springfield, Mo., for two months; transferred to Mason General Hospital in Brentwood, Long Island, for a three month course in neuropsychiatry; after a few months at Longview, Texas, went to Camp Atterbury, Ind., where he joined the 331st medical battalion of the 106th Infantry division; arrived in England about the middle of November 1944; wounded in the battle of Ardennes, Dec. 21, 1944; reported dead on Dec. 23, 1944, aged 26, while a prisoner of the German government.

Correspondence

SURGICAL-PATHOLOGIC COOPERATION IN LOWERING OPERATIVE INCIDENCE OF SO-CALLED CHRONIC APPENDICITIS

To the Editor:—The great discrepancy that exists between the clinical diagnosis of chronic appendicitis and many apparent nonpathologic appendixes subsequently reported by some pathologists as chronic appendicitis presents a serious and challenging problem to all clinicians and especially to surgeons.

In no other field of surgery is there tolerated so flagrant a violation of diagnostic and pathologic fundamentals. The growth of this pernicious practice is due to three errors: First, inadequate and hasty study by the clinician. All too frequently we find the first and easiest diagnosis to be chronic appendicitis, whereas the correct approach would be to proceed on the basis that this is the last possible diagnosis and should be arrived at only after all studies and adequate consultations have ruled out other diseases which may easily simulate chronic appendicitis. Only after this are we justified in subjecting the patient to surgery. The wisdom of the phrase "Error is always in haste" is often apparent as we review diagnostic errors. Failure to carry out adequate diagnostic study is the clinician's responsibility.

The second error is the lamentable trend shown by many pathologists to report slight alteration from the normal pattern as a diseased appendix for no other apparent reason than the fact that it was removed surgically. In the majority of cases this same pathologist, without knowing the operative history or the surgeon, could call these specimens normal appendixes. This is the pathologist's responsibility.

The third error is the indifference or inability of the clinician and pathologist to review the surgical specimen which is found to be normal. The clinician profits immensely by wholesome discussion of his problem, and an occasional admission of a diagnostic error will help to develop his future clinical judgment. This is demonstrated by the successful clinicopathologic conferences held today in many institutions. "From the errors of others a wise man corrects his own."

Although my own observations are limited to areas along the Eastern seaboard, the magnitude of this problem is well emphasized by the experience of the professor of medicine in one of our large Eastern medical colleges. After completing a transcontinental clinical trip he expressed alarm over the extraordinarily large number of appendectomies performed for chronic appendicitis through the entire country.

A pathologist in a distant community recently finished a study on a series of 335 appendixes removed for acute and chronic appendicitis. Of this group 72 per cent definitely showed gross and microscopic changes justifying the preoperative diagnosis. The remaining 28 per cent that did not show demonstrable disease was broken down for more critical analysis, using a code for each surgeon in order to maintain a critical attitude. The results showed beyond the slightest doubt that the better qualified surgeon removed infinitely fewer so-called chronic appendixes.

One institution has succeeded in reducing the rate of operative procedures for chronic appendicitis from 46 per cent to 10 per cent within the space of a few months by application of the aforementioned criteria for diagnosis; it would seem that this example might well be followed by many more hospitals.

EDWIN J. GRACE, M.D., Brooklyn.

NEOSTIGMINE METHYLSULFATE FOR PREECLAMPSIA

To the Editor:—The employment of neostigmine in the treatment of preeclampsia as suggested by Woodbury and his associates in THE JOURNAL, June 23, is based on principles underlying recent orientation on the etiology of the late toxemia of pregnancy (Hofbauer, J. I.: *West. J. Surg.* **49**:615 [Nov.] 1941; *Cincinnati J. Med.* **23**:107 [May] 1942; *Am. J. Surg.* **45**:361 [Sept.] 1944). The many theories advanced during past decades have failed to receive obstetric approval elucidating the true nature of the disorder.

While in the past the placenta was generally considered the chief characteristic of the pregnant state and, in toxemia, the principal factor responsible for the elaboration of "toxins," the new tenet inclines to the view that the pregnant state is essentially conditioned by the altered basic endocrine pattern. Notable among the hyperplastic changes occurring in the ductless glands during pregnancy are the phenomena in the adrenal cortex, the thyroid and the anterior hypophysis. In the present discussion the demonstration of increased secretion of the basophils during the last trimester of normal gestation and of cortical structures has first call in view of the clinical evidence that the adrenal cortex as well as the pituitary basophils may serve as factors in the genesis of hypertension (Rinehart, J. F.; Williams, O. O., and Cappeller, W. S.: Adenomatous Hyperplasia of the Adrenal Cortex Associated with Essential Hypertension, *Arch. Path.* **32**:169 [Aug.] 1941. Selye, Hans; Rowley, E. M., and Hall, C. E.: *Canad. M. A. J.* **49**:88 [Aug.] 1943). These factors, in conjunction with augmented reactivity of the arterioles to pitressin as the result of the presence during pregnancy in the blood of placental sex hormones in concentrations far above anything occurring in the nonpregnant state, serve as a basis for the appreciation of a delicately adjusted equilibrium between the opposing effects on the blood pressure of the endocrine factors and placental acetylcholine. A disturbance of this balance in toxemia was demonstrated by the reports of my associates of remarkably low acetylcholine values in 28 placentas and by the evidence adduced by Mukherjee of increased concentration in the blood of postpituitary principles in toxemia. These investigations have brought into clear relief the etiologic relationship between undue pitressin effects and the causation of toxemia. To the summation of the experimental, morphologic and chemical facts pointing in this direction, as recorded in previous communications, may be added the recent demonstration of the blood concentrating effect and of the phosphorus raising action of the pressor hormone by Stehle and Bourne (*J. Physiol.* **64**:229).

The cardinal aspects which enter into the rational therapy of preeclampsia entail primarily the preservation as far as possible of the functional integrity of the liver as the organ most concerned with the excretion and detoxication of pitressin and thyroxine. In view of my observations of the effects of neostigmine, which closely parallel the report of Woodbury, I hesitate to recommend this drug. There is, however, another consideration concerning the potentiation of naturally occurring placental acetylcholine by inhibiting cholinesterase. The most valuable sedatives in the treatment of eclampsia (morphine, barbiturates) strongly inhibit cholinesterase, as recently shown by the studies of E. A. Zeller (*Helv. chim. acta* **26**:1619, 1943) and F. Schütz (*J. Physiol.* **102**:259 [Dec. 31] 1943). Their empirical clinical use in eclampsia may thus be rationalized.

J. I. HOFBAUER, M.D., Cincinnati.

THE SUPPLY OF LABORATORY SERVICE

To the Editor:—In THE JOURNAL, June 16, page 539, Dr. Theodore Curphey criticized Montgomery County's method of supplying medical laboratory service to the public. His main objections were that: 1. If put into practice throughout the state and in other states, the system would "seriously jeopardize the healthy and natural development that laboratory medicine is now enjoying." 2. It would "limit the freedom of choice of the younger pathologist and would tend to force him into seeking state laboratory appointments." 3. It would "place at a serious economic disadvantage those private pathologists who work in proprietary hospitals or have laboratories of their own and who engage in private practice." 4. "These two things would be serious deterrents to the entry into the specialty of pathology by younger men." 5. The public's appreciation of pathologic services would be weakened because it is free. 6. "It might be harmful also to organized medicine in that . . . attempts might be made to offer the services of other medical specialists on the same basis to the community."

The first two of these objections are apparently based on a misapprehension of the facts. The Montgomery County Laboratory is not a state laboratory. It is entirely under county control. The expenses are paid jointly by the county and by the state. The intention of the state is, I believe, to encourage counties to supply laboratory service in those communities where it does not exist. Such communities are likely to be those whose population is too small to support the private practice of a pathologist and too distant from large centers to utilize existing facilities. By combining public health, hospital, medicolegal and outpatient work in one laboratory there may be enough to absorb the full time and interest of a pathologist, as in Montgomery County. It is desirable that most laboratory specimens be examined soon after collection, that the pathologist be familiar with local conditions and that he be available as a consultant. Furthermore, in many cases he needs information as to the clinical features. All this can be accomplished only if the laboratory is close to the community it serves.

While the Montgomery County type of laboratory is particularly suited to our community, this does not mean that it should be adopted in larger, more densely populated, areas or in places where satisfactory laboratory service is in existence. There is no danger that such a system will be "put into practice throughout the state and perhaps also in other states," nor does the New York State Department of Health propose to do so. It only provides aid to those communities which decide that they need it.

It will also be seen that objection 3 has no application to Montgomery County, for it was precisely the lack of private pathologists that incited the county to establish its laboratory. Indeed, the introduction of laboratory service where it is lacking creates additional positions for pathologists.

Objection 4 would be extremely serious if it should be corroborated. Before deciding what would deter younger men from entering the specialty of pathology, it would be desirable to ask the younger men that question. In my opinion there are at present two extremely serious and widespread deterrents to the specialty of pathology. The first is the low remuneration of pathologists in comparison to other physicians of equal training and degree of specialization. But this is at least as true of pathologists working in voluntary hospitals as of those employed in organizations such as the Montgomery County Laboratory. The second is the exclusion of pathologists from medical boards and generally from the direction of medical affairs in many hospitals. In Montgomery County the pathologist is a member of the staff of the two voluntary hospitals and has as much say in the government of the hospitals as the other physicians. The foregoing two factors being equal, I can see no reason for supposing that the type of administrative organization, whether hospital or county laboratory, would make the least difference to a young physician in deciding whether to enter pathology or another specialty.

Objection 5 deals with imponderables. As far as Montgomery County goes, my impression is that the public has shown at least as much appreciation of the free service as has been shown for paid services in other communities with which I am familiar.

Objection 6 can be judged only by the facts. In this county no such attempt has been made or, to my knowledge, even suggested. The county medical society was consulted and approved the laboratory plan before it was adopted.

Dr. Curphey concludes that a solution of the matter should be "motivated by a sincere desire to give an all inclusive modern laboratory service to communities, on a basis of individual community needs and not as is recommended in the Montgomery County Plan, as an overall free public service." All inclusive modern laboratory service on a basis of individual community needs is precisely what has been supplied in Montgomery County.

Finally, Montgomery County has made a contribution to pathologic service to the community which is worth pointing out. This is the recognition of autopsies as a vital public health service. In this county, autopsies are performed freely, not only, as in most places, on cases in which death has occurred in hospitals or medicolegal cases but on nonhospitalized cases as well. In addition to the public health value of this arrangement, it aids in research requiring prolonged follow-ups, as in cancer therapy. The possession of clinical and postmortem records of entire families in one laboratory also fosters the study of human genetics, a subject which should logically be within the province of pathology.

A. F. LIBER, M.D., Amsterdam, N. Y.
Director, Montgomery County Laboratory.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Malpractice: Alleged Failure to Sterilize Instruments Before Removing Pterygium from Eye.—The plaintiff consulted the physician defendant, an eye specialist, with respect to a growth in the corner of his left eye, which the physician diagnosed as a pterygium and advised its removal. Subsequently the physician performed the operation in his office in the presence of the plaintiff's aunt. Both the patient and his aunt testified that the physician "whetted" the instrument with which he operated "on a stone" and then proceeded to operate without either sterilizing the instrument or washing his own hands. This was denied by the physician. Subsequently a "severe infection" developed in the eye, and the patient sustained some loss of vision. Attributing the infection to the alleged failure of the physician to sterilize the instrument or to wash his hands immediately prior to operating, the patient instituted an action for malpractice against the physician. At the trial it was established that the operation performed by the physician was a minor one and when properly performed was ordinarily not followed by the result which here occurred; that for a physician to operate on an eye without washing his hands and sterilizing his instruments would constitute negligence; and that an infection in the part of the body operated on might result from the use of an unsterilized instrument. As stated before, the physician denied whetting the operating instrument on a stone and claimed to have sterilized the instrument and to have washed his hands immediately prior to operating. The physician and the medical witness called on his behalf both testified that instruments such as the defendant

used in the operation in question were not sharpened by the operators but came from the manufacturer already sharpened and in sealed packages. On the other hand, Dr. Kirkpatrick, another eye specialist practicing in the same vicinity, testified that he sharpened his instruments prior to an operation. The evidence adduced was in conflict as to the manner in which the patient's eye might have become infected. The defendant testified that he saw no evidence of infection in the patient's eye when he operated and he believed that after the operation the patient had taken the bandage off, suffered a fall or "gotten a lick" which caused the infection. The patient and other witnesses on his behalf denied that any such incident had occurred. A Dr. Fuller believed that the infection which caused the loss of vision in the patient's eye was probably in existence at the time of the operation. At the close of the evidence the trial court refused to direct a verdict in favor of the physician and after the jury returned a verdict for the patient refused to set that verdict aside. The physician then appealed to the Supreme Court of Arkansas.

In considering the question, said the Supreme Court, of the correctness of the action of the trial court in refusing to direct a verdict in favor of the physician and in refusing to set aside the verdict that was rendered by the jury in favor of the patient, this court must bear in mind these fundamental rules: 1. A court on appeal from a judgment based on a jury's verdict does not pass on the credibility of witnesses. That function is solely to be exercised by the jury, whose decision as to the credence to be given to testimony (except as to testimony contrary to scientific knowledge and mathematical facts) is binding on the appellate court. 2. Where the verdict is supported by any substantial testimony it must, in the absence of prejudicial errors of the trial court, be upheld; and in determining whether there is substantial testimony to support the verdict the evidence must be given the strongest probative force in favor of the party obtaining the verdict that it will reasonably bear. We conclude that, when the testimony in this case is considered in the light of these rules, it must be held that a fact question for the jury was presented by the evidence and that the jury's verdict is supported by substantial testimony.

The physician contended that the evidence was insufficient to justify the verdict, arguing that the charge of negligence against him was not supported by the testimony of any medical expert witnesses. He contended that in a case of this kind negligence cannot be established except by witnesses who are skilled in the practice of medicine. If, answered the court, there could, under the testimony, be any dispute as to the method used in the operation or in the treatment of the patient it would be necessary to establish the correct method by the testimony of medical witnesses but we do not have that situation here. There was no dispute whatever as to what was the proper course to be pursued by the physician in preparing for and performing the operation. It was not denied that it was necessary and proper for the physician to cleanse his hands thoroughly and to sterilize his instruments. The dispute in this case was as to whether or not the physician followed the course which is conceded to be necessary and proper. The physician testified that he did and the patient and his aunt testified that he did not follow this course. No amount of expert testimony could have thrown any light whatever on the real question in this case.

The physician further contended that, even if it be conceded that he failed to sterilize his instruments and to wash his hands, those facts were not sufficient on which to base a finding that such negligence was the proximate cause of the infection. It is not required in a case of this kind, said the court, that the injured party show to a mathematical certainty or to the exclusion of every other hypothesis that his injury occurred as a result of the negligence of which he complains. Herzog, in his "Medical Jurisprudence," discussing the quantum of proof necessary to sustain a recovery for malpractice, lays down this rule:

"It is not necessary to prove beyond a shadow of a doubt that an injury was caused by negligence preceding it, but a showing of strong probability of the causal relation is sufficient. . . . Where negligence and injury are proved, a causal connection between them may be established by circumstantial evidence, by inferences from physical facts" (pp. 161, 162, sec. 186).

In this case it was shown by testimony accepted as true by the jury that the physician failed to wash his hands and to sterilize his instruments before operating on the patient's eye. It was undisputed that a serious and unusual infection followed the operation. Since it appeared that all the causes for this infection, which were suggested by the physician and the medical witnesses called by him, were excluded by testimony which the jury had a right to believe, we conclude that the jury was authorized to find that the infection in the patient's eye was caused by the negligence of the physician.

Accordingly, the judgment in favor of the patient was affirmed.—*Lanier v. Trammell, 180 S. W. (2d) 818 (Ark., 1944).*

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

NATIONAL BOARD OF MEDICAL EXAMINERS EXAMINING BOARDS IN SPECIALTIES

Examinations of the National Board of Medical Examiners and Examining Boards in Specialties were published in THE JOURNAL, Aug. 4, page 1046.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: January. Sec., Dr. B. R. Austin, 519 Dexter Ave., Montgomery 4.

ALASKA: Juneau, September. Sec., Dr. W. M. Whitehead, Box 561, Juneau.

ARKANSAS: * *Medical.* Little Rock, Sept. 20-21. Sec., Dr. L. J. Kosminsky, Texarkana. *Eclectic.* Little Rock, Nov. 8. Sec., Dr. C. H. Young, 1415 Main St., Little Rock.

CALIFORNIA: *Oral.* San Francisco, Nov. 11. *Written.* Los Angeles, Aug. 13-16. Sec., Dr. Frederick N. Scatena, 1020 N St., Sacramento 14.

DISTRICT OF COLUMBIA: * *Reciprocity.* Washington, Sept. 10. Sec., Commission on Licensure, Dr. G. C. Ruhland, 6150 E. Municipal Bldg., Washington.

ILLINOIS: Chicago, Oct. 9-11. Supt. of Registration, Department of Registration & Education, Mr. Philip Harman, Springfield.

INDIANA: Indianapolis, Aug. 28-30. Sec., Board of Medical Registration & Examination, Dr. W. C. Moore, 301 State House, Indianapolis 4.

LOUISIANA: New Orlears, Aug. 16-18. Sec., Dr. R. B. Harrison, 1507 Hibernia Bank Bldg., New Orleans 12.

MARYLAND: *Homeopathic.* Baltimore, Dec. 11-12. Sec., Dr. J. A. Evans, 612 W. 40th St., Baltimore.

MONTANA: Helena, Oct. 1-3. Sec., Dr. O. G. Klein, First Nat'l. Bank Bldg., Helena.

NEW JERSEY: Trenton, Oct. 16-17. Sec., Dr. E. S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: * Santa Fe, Oct. 8-9. Sec., Dr. LeGrand Ward, 141 Palace Ave., Santa Fe.

NEW YORK: Albany, Buffalo, New York and Syracuse, Oct. 1-4. Sec., Dr. Jacob L. Lochner, Education Bldg., Albany.

SOUTH CAROLINA: Columbia, Nov. 13. Sec., Dr. N. B. Heyward, 1329 Blanding St., Columbia.

WISCONSIN: * Madison, Jan. 8-10. Sec., Dr. C. A. Dawson, Tremont Bldg., River Falls.

WYOMING: Cheyenne, Oct. 1-2. Sec., Dr. G. M. Anderson, Capitol Bldg., Cheyenne.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

COLORADO: Denver, Sept. 5-6. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver.

CONNECTICUT: Oct. 13. Address State Board of Healing Arts, 250 Church St., New Haven 10.

DISTRICT OF COLUMBIA: Washington, Oct. 22-23. Sec., Commission on Licensure, Dr. G. C. Ruhland, 6150 E. Municipal Bldg., Washington.

FLORIDA: DeLand, Nov. 3. Sec., Dr. J. F. Conn, Box 655, DeLand.

IOWA: Des Moines Oct. 9: Dir., Division of Licensure and Registration, Mr. H. W. Grefe, Capitol Bldg., Des Moines.

MICHIGAN: Ann Arbor and Detroit, Oct. 12-13. Sec., Miss Eloise LeBeau, 101 N. Walnut St., Lansing.

MINNESOTA: Minneapolis, Oct. 2-3. Sec., Dr. J. C. McKinley, 126 Millard Hall, University of Minnesota, Minneapolis 14.

NEBRASKA: Omaha, Oct. 2-3. Dir., Bureau of Examining Boards, Mr. Oscar F. Humble, 1009 State Capitol Bldg., Lincoln 9.

RHODE ISLAND: Providence, Aug. 15. Chief, Division of Examiners, Mr. Thomas Casey, 366 State Office Bldg., Providence.

SOUTH DAKOTA: December. Sec., Dr. J. D. Alway, Aberdeen.

TENNESSEE: Memphis, Sept. 24-25. Sec., Dr. O. W. Hyman, 874 Union Ave., Memphis.

WISCONSIN: Madison, Sept. 22. Sec., Prof. R. N. Bauer, 152 W. Wisconsin Ave., Milwaukee 3.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1935 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Ophthalmology, Cincinnati

28:581-700 (June) 1945

Sympathetic Ophthalmia Following Subconjunctival Rupture of Eyeball. C. A. Perera.—p. 581.
Wernicke's Disease (Encephalitis Hemorrhagica Superioris). D. Kravitz and R. H. Stockfisch.—p. 596.
Angioid Streaks in Deep Layers of Retina. A. J. Bedell.—p. 601.
*Diabetic Iridopathy. C. A. Clapp.—p. 617.
Onchocerciasis: A Study of Ocular Complications in 342 African Cases. J. G. Scott.—p. 624.
*Recurrence of Tobacco-Alcohol Amblyopia. F. D. Carroll.—p. 636.
Visual Disturbance After Ingestion of Digitalis. H. M. Langdon and R. D. Mulberger.—p. 639.
Concerning Early Ocular Symptoms of Multiple Sclerosis. C. A. Veasey. —p. 640.
On Biastigmatism. J. I. Pascal.—p. 644.

Diabetic Iridopathy.—According to Clapp, diabetic conditions are sometimes associated with changes in the iris. Some of these changes are inflammatory, but the majority are not associated with inflammation and should be designated as iridopathy. These noninflammatory changes may be confused with malignant melanoma. Practically all of the pathologic material available to Clapp showed severe changes in the pigment epithelial layer. He presents 2 case histories and reproduces a number of photomicrographs showing changes in the pigmented layer of the iris. These changes deserve further study in order to ascertain whether they are limited chiefly to diabetic patients and also their cause.

Tobacco-Alcohol Amblyopia.—Carroll reports the case of a woman with tobacco-alcohol amblyopia who regained normal vision and normal fields, although she did not decrease her alcoholic intake or improve her diet. Vitamin B appeared to be responsible for the satisfactory results. When the thiamine was discontinued the amblyopia recurred, and when it was used again essentially normal vision was obtained. The author thinks, however, that it is advisable to use a good diet supplemented by the whole vitamin B complex as well as just vitamin B_1 for the best results in the treatment of this condition.

Am. J. Syphilis, Gonorrhea and Ven. Dis., St. Louis

29:281-380 (May) 1945

Problem of Infection of Animal Mucosae with Neisseria Gonorrheae: I. Modification of Host Resistance. J. H. Hill, Virginia Huffer and Ellen Nell.—p. 281.
*False Positive Serologic Reactions for Syphilis, with Special Reference to Those Due to Smallpox Vaccinations (Vaccinia). C. R. Rein and Elizabeth S. Elsberg.—p. 303.
Penicillin in Late Syphilis: Interim Report. J. H. Stokes, with collaboration of H. Beerman, N. R. Ingraham Jr. and others.—p. 313.
*Penicillin Therapy of Sulfonamide Resistant Gonococcic Infections and Associated Complications in the Male: Schedule of Treatment for Ambulatory Patients. A. Cohn and B. A. Kornblith.—p. 334.
Case of Yaws in White American Soldier. L. Katzenstein.—p. 340.
Time-Dose Relationships of Penicillin Therapy: III. Regimens Used in Early Syphilis. W. McDermott, Maria Benoit and Rebeckah DuBois. —p. 345.
U. S. Army Experiences in Venereal Disease Control in European Theater of Operations. P. Padget.—p. 352.
Keratoderma Blennorrhagicum: Brief Review and Report of Case Treated with Penicillin. E. M. Satulsky.—p. 361.

False Positive Serologic Reactions for Syphilis Due to Smallpox Vaccinations.—Rein and Elsberg investigated the nature and incidence of false positive serologic reactions for syphilis following smallpox vaccinations. All soldiers were examined one week after they received smallpox vaccination, and those who developed a vaccinoid or vaccinia reaction were referred for serologic investigation. All specimens were subjected to the Kline diagnostic, Kline exclusion, Boerner-Jones-Lukens, Mazzini and Kahn standard flocculation tests and the Kolmer complement fixation test. One hundred and twenty-nine soldiers developed a vaccinoid or vaccinia reaction following the smallpox vaccination, of whom 58 (44.9 per cent) showed doubtful or positive tests with one or more of the serodiagnostic procedures employed. The authors stress that, since biologic false positive reactions occur with some frequency following smallpox vaccinations, it is important to rule out that possibility before antisyphilitic treatment is instituted. Irreparable physical and psychologic damage has been produced by an ill considered or hasty diagnosis. If treatment is started prematurely, the evidence which could have finally led to an accurate diagnosis is often obscured. Serologic tests may become negative with a small amount of treatment, and one is at a loss to know whether the seronegativity represents a response to therapy or merely reflects the fact that the patient has never had syphilis. Much time can be saved by thoroughly studying the soldier with an unexplainable positive serologic reaction before the diagnosis of syphilis is established and treatment is instituted.

Penicillin Therapy of Sulfonamide Resistant Gonococcic Infections.—Cohn and Kornblith employed penicillin in the treatment of 113 men with sulfonamide resistant gonococcic infections. Two schedules of penicillin therapy were tested. In both schedules a total dosage of 100,000 Oxford units of penicillin, administered intramuscularly, was found both necessary and sufficient for bacteriologic cure. In the first schedule, treatment was divided over a period of six hours; an initial injection of 50,000 Oxford units of penicillin was followed by two intramuscular injections of 25,000 Oxford units each at three hour intervals. Eleven patients who received this schedule of therapy became bacteriologically negative within four hours, and in the second schedule of treatment 102 patients received the total amount of 100,000 Oxford units of penicillin within a period of four hours. A total of 100 cases in this group responded promptly to one course of therapy. Eight of these patients were reinfected, and 5 of them again responded to a second course of penicillin therapy. Of the 113 cases studied, 94 (83 per cent) presented complications. There were 8 cases of epididymitis and 86 cases of prostatitis. The acute symptoms of epididymitis, such as pain, fever and malaise, subsided within three days among 7 of the 8 cases observed. Swelling and induration of the epididymis and inflammatory hydrocele persisted for variable periods of one to four weeks. Acute symptoms and signs of prostatic involvement subsided promptly after penicillin therapy. The more chronic infiltrations improved moderately during five weeks of observation. There was no consistent correlation between the clinical findings in the prostate and the corresponding microscopic findings of wet smears from prostatic secretions. Reactions to penicillin therapy were of a mild and transitory character. The authors conclude that the therapy of complications of gonococcic infections does not necessarily end with the administration of the penicillin alone.

American Review of Tuberculosis, New York

51:393-488 (May) 1945

*Minimal Tuberculous Lesions of Lung: Their Clinical Significance. D. Reisner and J. Downes.—p. 393.
Tuberculosis Mortality in Communities of Different Size. J. Yerushalmy and Charlotte Silverman.—p. 413.
Ventilatory Function: Experiences with Simple Practical Procedure for Its Evaluation in Patients with Pulmonary Tuberculosis. F. C. Warring Jr.—p. 432.
Bronchography in Pulmonary Tuberculosis: IV. Geographic Adventure —Part I. B. A. Dormer, J. Friedlander and F. J. Wiles.—p. 455.
*Diasone Therapy of Pulmonary Tuberculosis: Its Clinical Efficacy and Toxicity. L. Benson and L. Goodman.—p. 463.
Fatal Pemphigoid Reaction to Diasone. E. H. Robitzek.—p. 473.
Tuberculin Testing of Medical Students: Reaction to Tuberculin of Second Year Medical Students at College of Physicians and Surgeons, Columbia University. M. M. Steinbach and C. J. Duca.—p. 478.

Minimal Tuberculous Lesions of Lung.—Reisner and Downes studied the behavior of the minimal lesion of tuberculosis during a period of about five years, which was the length of time for which about 50 per cent of the patients were followed up, the others being observed for longer or shorter periods. The material was collected from the ambulatory chest

clinics of the New York City Department of Health and consists of 469 persons, of whom 200 were male and 269 female. Since analysis by sex showed no indication that females were more liable to progressive disease than males, the data for the two sexes have been combined. None of the patients were less than 10 years of age, 24 per cent were between 10 and 25, 58 per cent were in the age group between 25 and 44 and 18 per cent were 45 years or older. The majority of patients showing involvement of minimal extent are asymptomatic and aside from roentgenologic findings present few objective criteria for evaluation of their clinical significance. An appraisal of the clinical importance and presumable prognosis of the minimal tuberculous lesion requires a qualitative differentiation of the type of lesion. Lesions of the exudative or exudative-productive type are characterized by an unstable behavior and a tendency to progression. Progression was observed in about one half of the white patients and in 61 per cent of the nonwhite patients. Lesions of productive-fibrotic or fibrocalcific character have shown a stationary behavior in the majority of instances, progression or instability having occurred in only 5 per cent of the white and 14 per cent of the nonwhite patients. Lesions of the fibrocalcific type showed the highest rate of stability, progression being an exceptional occurrence. If the character of the lesion is considered, age per se is not important as far as the risk of developing progressive disease is concerned. The age factor merits consideration from the point of view of prognosis to the extent that lesions of exudative character, representing a presumably early and potentially progressive type of involvement, are more apt to be found in the young age groups. Supervision of patients with minimal tuberculosis should be on a selective basis and should take into account the risk of progressive disease as related to the character of the lesion.

Diasone Therapy of Pulmonary Tuberculosis.—Benson and Goodman administered diasone for from 120 to 160 days to 22 patients with pulmonary tuberculosis. Only 4 patients may possibly have benefited from the drug. Two patients in the series died while on the diasone therapy. Another patient developed an exfoliative dermatitis necessitating withdrawal of the drug. A variety of toxic and untoward responses to diasone were observed, including cyanosis, anemia, dermatitis, fever, jaundice, tremors, diplopia and enlargement of the thyroid. Diasone is an experimental drug which is currently being investigated. It should be employed only under the most rigid clinical and laboratory control.

Archives of Internal Medicine, Chicago

75:279-356 (May) 1945

Brain Abscess Associated with Congenital Heart Disease. S. L. Robbins. —p. 279.
*Influence of Anoxemia on Hemopoietic Activity. A. Hurtado, C. Merino and E. Delgado.—p. 284.
Effects of Some Liver Extracts on Carbohydrate Metabolism. H. B. Sokal.—p. 324.
Effects of Some Liver Extracts on Carbohydrate Metabolism. J. E. Sokal.—p. 327.
Gastroenterology: Review of Literature from July 1943 to June 1944. W. L. Palmer, D. S. Harman and W. E. Ricketts.—p. 341.

Anoxemia and Hemopoietic Activity.—Hurtado and his associates describe investigations of the influence of temporary, intermittent and chronic anoxic anoxia (anoxemia) on the morphologic and other characteristics of the circulating blood of several series of healthy and diseased male subjects at sea level and various altitudes. They found that exposure to a low pressure environment causes a polycythemic response. In general the level of polycythemia is directly proportional to the degree, duration and continuity of the anoxic stimulus. There seems to be a limit for the hematologic response to the anoxic stimulus. When this is extremely severe a decrease rather than a further increase is observed in polycythemia. The level of hemoglobin in the circulating blood may be one of the many factors which tend to preserve the internal stability against the disturbing influence of a constant lowering of the oxygen tension in the inspired air. The polycythemia associated with the anoxemia of high altitudes is absolute in type. The elevation in the total blood volume, which at times reaches high values, is due to an increased red cell volume. The polycythemia observed on arrival at high altitudes seems to be due to release of stored blood and hemoconcentration; that corresponding to a repeated or constant exposure to a low pressure environment is related to an erythropoietic hyperactivity. The polycythemia associated with a constant or intermittent anoxemia tends to show a proportional elevation in the circulating reticulocytes and in the serum bilirubin. The latter characteristic suggests that an increased rate of cellular destruction parallels the increased formation, but other factors, such as insufficiency of the liver in excretion of pigment, due to the anoxic condition, may also be a factor in the hyperbilirubinemia. The stimulating influence of anoxemia on the hemopoietic system is restricted to the formation of red blood cells and hemoglobin. Leukopoietic activity is not affected. Chronic anoxemia does not modify the erythropoietic activity permanently. When a person who has lived since birth at high altitudes is brought down to sea level he shows after some time blood characteristics similar to those found in persons who have always lived under the latter environmental conditions. Comparative study of the polycythemia of high altitudes and the polycythemic processes observed at sea level indicates that (*a*) in cases of anoxemia at sea level due to pulmonary changes the polycythemic response tends to be less than with corresponding degrees of arterial oxygen unsaturation at high altitudes, except in cases of Ayerza's disease; (*b*) it is not likely that the causative mechanism of polycythemia vera is related to the existence of an anoxic stimulus.

Archives of Ophthalmology, Chicago

33:341-428 (May) 1945

Inherited Cataract in the B. Genealogy: Occurrence of Diverse Types of Cataract in Descendants of One Person. F. C. Lutman and J. V. Neel.—p. 358.
Surgical Management of Glaucoma in Correlation with Gonioscopy and Biomicroscopy. S. J. Meyer and P. Sternberg.—p. 358.
Pathologic Physiology of Convergent Strabismus: Motor Aspects of Nonaccommodational Type. F. H. Adler.—p. 362.
Use of Methyl Cellulose in Ophthalmology. K. C. Swan.—p. 378.
Ophthalmic Prisms: Corrective and Metric. L. G. H. Hardy, R. R. Chace and M. C. Wheeler.—p. 381.
*Ocular Sequelae of Administration of General Anesthesia: Paralysis of the Superior Rectus Muscle, Exophthalmos, Pseudoptosis and Fibrosis of the Inferior Rectus Muscle Following an Operation for Pilonidal Cyst with Patient Under General Anesthesia. C. Berens and G. Fonda. —p. 385.
Glaucoma Associated with Nevus Flammeus: Report of Case. E. E. Grossman.—p. 389.
Pathogenesis of Glaucoma. L. Hess.—p. 392.
Ophthalmologic Features of Intracranial Chordoma and Allied Tumors of the Clivus. I. Givner.—p. 397.
Use of Troncoso's Magnesium Implant in Cyclodialysis for Relief of Glaucoma: Observations in 2 Cases. P. H. Boshoff.—p. 404.

Ocular Sequelae of General Anesthesia.—Berens and Fonda report the case of a man aged 26 who was operated on for pilonidal cyst under ethylene-ether anesthesia. Prior to this operation the patient's eyes revealed no abnormality. Within twenty-four hours after the operation the patient experienced diplopia when looking upward. On the following day the diplopia was present while he was reading. Onset of ptosis was coincidental with the diplopia. Later examinations revealed paralysis of the superior rectus muscle, exophthalmos, pseudoptosis and fibrosis of the inferior rectus muscle. The most probable explanation of the ocular symptoms was that an embolism of the artery supplying the superior rectus muscle occurred. Fibrosis of the inferior rectus muscle may have been caused by the secondary contracture associated with embolic myositis. There may be no proved causal relationship between the ethylene-ether anesthesia and the sudden onset of diplopia and the proptosis, but the short interval of less than twenty-four hours between the occurrence of the ocular symptoms and the operation is highly suggestive of a close relationship.

Delaware State Medical Journal, Wilmington

17:81-110 (May) 1945

Psychiatry in Postwar Era. M. A. Tarumianz.—p. 81.
Atypical Case of Cerebellar Tumor. P. F. Elfeld.—p. 87.
Psychiatric Problems of Service Men's Wives. B. G. Lawrence.—p. 89.
The Psychic Epileptic Variant. G. J. Gordon.—p. 90.
Role of Insufficient Laboratory Study and Inadequate Treatment in Development of General Paresis. M. B. Zimbler.—p. 93.
Differential Diagnostic Considerations in Case of Postinfectious Psychosis. G. S. Bieringer.—p. 97.
Religious Sexual Excitement Syndrome in Schizophrenic Minister. F. A. Freyhan.—p. 99.
Treatment of Expressive Aphasia in War Veteran. J. Jastak.—p. 101.

Journal of Clinical Endocrinology, Springfield, Ill.

5:163-202 (April) 1945

Treatment of Adrenal Insufficiency. R. H. Williams, J. L. Whittenberger, G. W. Bissell and A. R. Weinglass, with the technical assistance of J. B. Peters.—p. 163.
Protein Bound Plasma Iodine in Patients with Thyroid Disease: Effect of Thiouracil. B. E. Lowenstein, M. Bruger, J. W. Hinton and W. G. Lough, with the technical assistance of S. Member.—p. 181.
Premature Sexual Precocity in a Young Girl. K. J. Karnaky.—p. 184.

Journal of Immunology, Baltimore

50:255-316 (May) 1945

Relative Susceptibility of Normal and X-Rayed Mice of Different Stocks to Pneumococcic Viruses. P. F. de Gara and J. Furth.—p. 255.
In Vitro and In Vivo Activity of Synthetic Detergents Against Influenza A Virus. M. Klein and D. A. Stevens.—p. 265.
Development of Acute Immunity in Swiss Mice with Infective and Noninfective Suspensions of Poliomyelitis Virus. S. D. Kramer and H. A. Geer.—p. 275.
Immunologic Studies on Fibrin. K. C. Robbins.—p. 283.
Concentration and Purification of Influenza Virus for Preparation of Vaccines. A. R. Taylor, D. G. Sharp, I. W. McLean Jr., Dorothy Beard and J. W. Beard.—p. 291.

Journal of Infectious Diseases, Chicago

76:83-162 (March-April) 1945

Infection of Ticks (Dermacentor Variabilis) with Pasteurella Tularensis. J. F. Bell.—p. 83.
Immunologic Studies on Psittacosis-Lymphogranuloma Group of Viral Agents. M. R. Hilleman.—p. 96.
Field Study of Latent Tularemia in Rodents with List of All Known Naturally Infected Vertebrates. A. L. Burroughs, R. Holdenried, D. S. Longanecker and K. F. Meyer.—p. 115.
Effect of Chlorination on Virus of Eastern Equine Encephalomyelitis in Presence of Organic Substances. J. E. Kempf, Marjorie E. Pierce, Martha G. Wilson and M. H. Soule.—p. 120.
Studies on Endameba Histolytica: V. On Decrease in Infectivity and Pathogenicity for Kittens of E. Histolytica During Prolonged In Vitro Cultivation and Restoration of These Characters Following Encystment and Direct Animal Passage. Shih Lu Chang.—p. 126.
Isolation of Agent Belonging to Psittacosis-Lymphogranuloma Group of Viruses. Alice H. Kempf, A. H. Wheeler and W. J. Nungester.—p. 135.
Trypanocidal Activity and Toxicity of Antimonials. G. Chen, E. M. K. Geiling and R. M. MacHatton.—p. 144.
Effect of Cysteine on Trypanocidal Activity and Toxicity of Antimonials. G. Chen, E. M. K. Geiling and R. M. MacHatton.—p. 152.
Susceptibility of Muskrats and Other Rodents to Poliomyelitis Virus (Lansing Strain). F. B. Gordon.—p. 155.

Laryngoscope, St. Louis

55:191-238 (May) 1945

Surgery of Facial Nerve in 300 Operated Cases. T. G. Tickle.—p. 191.
*Surgical Treatment of Cancer of Larynx. C. L. Jackson and C. M. Norris.—p. 196.
Use of Otosmosan in Otology: Clinical Report. S. J. Kopetzky.—p. 216.
Abscesses of Pyriform Sinus. A. Nigro.—p. 228.

Cancer of Larynx.—Cancer of the larynx is 100 per cent fatal without treatment, but according to Jackson and Norris the prognosis of treated cases is better than in cancer of most other parts of the body. The cases treated surgically should be divided into those treated by laryngofissure (or partial laryngectomy) and those treated by total laryngectomy. The mortality of the form of laryngofissure used by the authors should be practically zero. In their clinic not a single patient has died of this operation for fourteen years; and during this time 148 laryngofissures have been done. According to the literature, the mortality of total laryngectomy is certainly much higher than that of laryngofissure, but in the last 70 laryngectomies performed by the authors there has not been a single operative fatality. A recent analysis of the end results in a series of 150 patients with cancer of the larynx treated at the Temple University Hospital by surgery and irradiation during the period 1930 to 1937 inclusive showed a combined five year cure rate of 64 per cent. Of the 101 patients with intrinsic lesions who underwent either laryngofissure or laryngectomy, 80 patients obtained at least a five year cure. Nine patients with extrinsic lesions in whom laryngectomy was done died. During the same period 34 patients were treated by irradiation (protracted fractional technic), 22 of them intrinsic and 12 extrinsic. In the intrinsic group a 59 per cent five year cure rate was obtained, in the extrinsic group a 25 per cent five year cure rate.

Maine Medical Association Journal, Portland

36:75-90 (May) 1945

Pudendal Block Anesthesia in Home Obstetrics. M. Trowbridge Jr.—p. 75.
Problem of Acute Gastrointestinal Hemorrhage. E. H. Risley.—p. 80.

36:91-116 (June) 1945

Acute Abdominal Emergencies. A. H. McQuillan.—p. 91.
Use of Prostigmine in Arrested Poliomyelitis. G. Geyerhahn.—p. 95.

New England Journal of Medicine, Boston

232:613-640 (May 24) 1945

The Circus Disaster and the Hartford Hospital. D. B. Wells.—p. 613.
Salicylism Accompanied by Respiratory Alkalosis and Toxic Encephalopathy: Report of Fatal Case. H. W. Ryder, M. Shaver and E. B. Ferris.—p. 617.
Endoscopy. E. B. Benedict.—p. 621.
Chronic Ulcerative Colitis; Acute Ulcerative Ileitis with Perforation. H. S. Pittman.—p. 628.
Rheumatoid Arthritis. Amyloidosis of Kidneys, Spleen and Liver. W. W. Beckman.—p. 632.

232:641-664 (May 31) 1945

*Ligation of Inferior Vena Cava in Prevention and Treatment of Pulmonary Embolism. E. E. O'Neil.—p. 641.
Cruveilhier-Baumgarten Syndrome: Case. A. Blain III and M. Clapper.—p. 647.
Eczema. F. M. Rackemann.—p. 649.
Acute Hepatitis. J. C. Aub.—p. 654.
Adenoacanthoma of Pancreas. F. D. Moore.—p. 657.

Ligation of Inferior Vena Cava in Pulmonary Embolism.—O'Neil suggests that when concurrent phlebothrombosis exists in both lower extremities and has extended to or above the inguinal ligament and when pulmonary embolism has occurred and its course is not evident, interruption of the inferior vena cava is indicated. The fact that aseptic thrombosis may exist in the large pelvic vessels and initiate a serious embolism should not be overlooked. If an operation is to be performed only on suspicion of deep venous thrombosis, the best assurance that can be given for the patient's safety is the highest possible ligation compatible with adequate venous return.

Surgery, Gynecology and Obstetrics, Chicago

80:561-662 (June) 1945

*Mechanism of Shock from Burns and Trauma Traced with Radiosodium. C. L. Fox and A. S. Keston.—p. 561.
Analysis of Massachusetts General Hospital Cases of Lung Abscess from 1938 Through 1942. R. H. Sweet.—p. 568.
*Postoperative Prophylaxis of Recurrent Mammary Cancer with Testosterone Propionate. A. Prudente.—p. 575.
Role of the Decompensatory Reaction of Peripheral Blood Vessels in Tourniquet Shock. B. W. Zweifach, R. G. Abell, R. Chambers and G. H. A. Clowes.—p. 593.
Effects of the Parenteral Administration of Fluids on Metabolism of Electrolytes During Postoperative Convalescence. E. M. Limbert, M. H. Power, J. D. Pemberton and E. G. Wakefield.—p. 609.
Treatment of Thrombophlebitis. M. D. Yahr, C. Reich and C. Eggers.—p. 615.
Surgical Anatomy of Facial Nerve, with Special Reference to the Parotid Gland. L. J. McCormack, E. W. Cauldwell and B. J. Anson.—p. 620.
*Causalgia. F. H. Mayfield and J. W. Devine.—p. 631.
Safe, Simple and Efficient Method of Intestinal Anastomosis. J. Peyton Barnes.—p. 636.
Transverse Upper Abdominal Incisions. M. S. Rosenblatt and D. Colver.—p. 641.
Primary Tumors of Liver. W. N. Warvi.—p. 643.

Mechanism of Shock.—Fox and Keston used radioactive sodium to explore whatever changes might occur after shock from burns or trauma. Two types of experiments were conducted. In one type animals were prepared with radiosodium given in isotonic solution of sodium chloride so that the body sodium was in equilibrium and tagged with the isotope. Shock was produced twenty hours later, and the concentration of radiosodium in the tissues and organs was determined in the animals during shock but not when moribund. In a second type of experiment shock was produced first and the animals were then treated with isotonic saline solution containing some radiosodium. About twenty hours later, on recovery from potentially fatal shock (as judged by death of untreated controls), the concentration of radiosodium was determined in tissues and organs. The water content of all tissues sampled was also measured by drying the tissues at 110 C. for eighteen to twenty-four hours. Similar analyses were performed in parallel control animals which had not been injured but which had received equal doses

of radioactive sodium. The experiments were made on mice. They demonstrated the great accumulation and side tracking of sodium in injured tissues with subsequent reduction in plasma volume characteristic of traumatic shock. Conversely, treatment with an amount of isotonic sodium solution approximating one-half the extracellular volume restored this volume. This explains the successful treatment of shock in animals and in man with large volumes of isotonic solutions of sodium salts.

Testosterone Propionate in Mammary Cancer.—Prudente used testosterone as a postoperative measure in treating 63 patients with mammary cancer who had previously been operated on. As controls, 64 cases are reported in which the breast had been removed by the same technic of radical surgery and in which testosterone propionate was not used. All 127 cases were operable. The results obtained, as gaged by the survivals of three, four and five years, are about 100 per cent better than those observed after operation only. This fact indicates that testosterone propionate exercises a protective or prophylactic action against recurrences of surgically treated mammary cancer. Very high doses of testosterone propionate, up to 175 mg. a week, may and should be used after operations for mammary cancer, and this treatment should be continued through many years. The principal criterion for the selection of the dosage is the grade of histologic malignancy of the tumor. The side effects following this therapy are of secondary importance. They consist of virilization and of disturbances of menstruation. In patients between 40 and 50 years of age who are still menstruating, early cessation of menstruation is often observed.

Causalgia.—Mayfield and Devine report 15 cases of causalgia found among a group of 737 peripheral nerve injuries. The nerve lesion was incomplete in each case of causalgia. This syndrome has not been seen in any individual in whom the nerve was completely divided. Burning pain was a constant complaint and was usually immediate in onset. The median or sciatic nerve was involved in each instance. Certain patients showed vasoconstriction in the causalgic limb; others showed vasodilatation. The trophic changes and response to warm or cold moisture and to hyperthermia varied, depending on the blood flow. Twelve patients were relieved by sympathectomy of the involved limb; 1 was cured by artificial fever therapy and 2 recovered spontaneously. Direct surgical attack (neurolysis) on the injured nerve, which was performed in 5 cases, and periarterial sympathectomy at the level of the injury, performed in 3, have not been of benefit. Procaine block of the sympathetic chain affords complete relief temporarily and should be repeated two to three times, although no case in this series has shown any lasting benefit from this procedure. Sympathectomy (preganglionic) gave immediate and lasting relief to 12 patients. Sympathectomy should be done early to prevent stiffness of joints due to disuse. The personality changes present during the painful stages are secondary to the pain. There is no evidence in these cases that there is a predisposing constitutional psychic factor in causalgia.

Union Médicale du Canada, Montreal

74:721-876 (June) 1945

Penicillin from Biologic and Experimental Point of View. A. Frappier.—p. 726.
*Rare Cause of Acute Intestinal Occlusion: Incarcerated Transmesenteric Hernia. E. Desjardins.—p. 734.
Total Gastrectomy. J. Bruneau.—p. 741.
Goiter and Psychosis. R. Dore.—p. 749.
Vesicovaginal Fistulas: 3 Cases. F. X. Demers and J. Fisher.—p. 753.
Spring and Summer Dermatoses. H. Smith.—p. 756.
Surgery of Pain: Painful Stumps and Their Treatment.—p. 764.

Transmesenteric Strangulated Hernia.—Desjardins presents the case of a man aged 47 who had always been in good health but who suddenly during the night had a violent attack of abdominal pain with vomiting. Examination revealed a severe state of shock, hypothermia, rapid pulse, muscular rigidity over the whole abdomen and the presence of a mass in the hypogastric region and the iliac fossae. On operation a strangulated transmesenteric hernia was found, 60 inches of the small intestine was resected and an ileocecal anastomosis was made. The postoperative course was stormy; there was a localized peritonitis, a pulmonary abscess and purulent pleurisy. A drainage pleurotomy was done, but the patient died thirty-nine hours after the onset of the disease. These hernias are not frequent, Hausmann and Morton having found only 52 cases among 467 cases of internal hernias. Diaphragmatic hernias are the most frequent among the internal types of hernia. The transmesenteric hernias may supervene at any age and in both sexes. They do not have a sac and consist only of the passage of a loop of intestine through a gap in the mesentery.

War Medicine, Chicago

7:275-340 (May) 1945

*Reaction of Degeneration in Electrodiagnosis of Experimental Peripheral Nerve Lesions. L. J. Pollock, J. G. Goldseth, A. J. Arieff, I. C. Sherman, M. A. Schiller and E. L. Tigay.—p. 275.
Subacute Emotional Disturbances Induced by Combat. R. A. Cohen and J. G. Delano.—p. 284.
*Functional Enuresis in the Army: Report of Clinical Study of 100 Cases. H. Shlionsky, L. R. Sarracino and L. J. Bischof.—p. 297.
Review of Gastroscopic Studies on 100 Consecutive Pre-Pearl Harbor Military Patients. C. A. Tavares.—p. 304.
Negro Army Psychiatric Casualties: Statistical Report on 100 Negro Soldiers Referred to an Army Mental Hygiene Unit. H. E. Harms, F. J. Kobler and F. J. Sweeney.—p. 309.
Classification for Medical Corps Officers of Army Air Forces. W. A. Glasier.—p. 313.

Reaction of Degeneration in Peripheral Nerve Lesions.—Pollock and his associates describe the data obtained from the examination of denervated and recovering muscles in cats as related to the characteristics of the reaction of degeneration; they compare such data with some obtained in human subjects and discuss the usefulness of the reaction of degeneration as a diagnostic and prognostic sign. For the most part Erb's description of the characteristics of complete reaction of degeneration have been confirmed by their studies. They emphasize that faradic stimulation is effective throughout degeneration, denervation and regeneration, provided sufficient amperage is employed. The changes of response to galvanic stimulation of "infinite time" which characterize complete reaction of degeneration are (1) hyperirritability of muscle to galvanic stimuli, (2) sluggishness of relaxation of the contraction wave, (3) lessening of the ratio between amperage necessary to produce tetanus and rheobase to almost unity and (4) increase of efficacy of the anodal closing stimulus to equality with the cathodal closing stimulus. Unequivocal signs of recovery are (1) a sudden increase in rheobase, (2) an increase of ratio between the amperage necessary to produce tetanus and rheobase and (3) an increase in efficacy of the cathodal closing stimulus as compared with the anodal closing stimulus. The electrical sign of recovery characterized by the sudden increase of rheobase antedates the recovery of motion and sensation for long periods, in man by many weeks. The other signs likewise antedate other clinical signs of recovery. Electrotherapy has no effect on the response of muscles to electrical stimuli.

Functional Enuresis in the Army.—Shlionsky and his co-workers report observations on 100 men with functional nocturnal enuresis whom they studied in an army training camp in the United States. They found that the educational and occupational background of these men was in general below average. Most of the men had lived in rural communities and had used outdoor toilets in childhood. There was a high incidence of enuresis in the immediate families of these soldiers. A considerable number gave a history of disruption of the home or of exposure to various other unfavorable types of environment in childhood. A relatively high percentage of the men were below average intelligence. The majority manifested in addition to the enuresis various neurotic tendencies and personality disorders. Most of the men showed evidence of emotional immaturity. Not infrequently there was persistence or recurrence of some of the various neurotic traits of childhood, such as nightmares, nail biting, stuttering, fear of the dark, sleepwalking and talking in the sleep. Functional backache was a common symptom. Virtually none of the patients had ever received adequate medical attention for the enuresis prior to army service. Functional enuresis is generally but one manifestation of a lifelong pattern of neurotic behavior or personality maladjustment and is not infrequently associated with adequate intelligence. Apart from the consideration that the symptom of enuresis itself creates a difficult situation in the service, it is apparent that the majority of enuretic adults do not possess the qualifications necessary for the successful performance of duty in the armed forces.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

Journal of Endocrinology, London

4:103-218 (Jan.) 1945

Effects of Sex Hormones on Blood in Rats. V. Korenchevsky and K. Hall.—p. 103.
Influence of Thyroid on Pregnancy and Parturition in Rabbit. J. P. Chu.—p. 109.
Role of Thyroid Gland and Estrogen in Regulation of Gonadotropic Activity of Anterior Pituitary. J. P. Chu and S. S. You.—p. 115.
Ovarian Stimulation by Estrogens: 2. Stimulation in Absence of Hypophysis, Uterus and Adrenal Glands. P. C. Williams.—p. 125.
Studies of Biologic Action of Serum Gonadotropin. P. C. Williams.—p. 127.
Adrenalectomy and Gastric Secretion. E. Tuerkischer and E. Wertheimer.—p. 143.
"Growth" in Relation to Diabetogenic and Pancreotropic Actions of Anterior Pituitary Extract. R. F. Ogilvie.—p. 152.
Experimental Control by Hormone Action of Estrous Cycle in Ferret. F. H. A. Marshall and J. Hammond Jr.—p. 159.
Induced Ovulation and Heat in Anestrous Sheep. J. Hammond Jr.—p. 169.
Induction of Lactation in Goats and Cows with Synthetic Estrogens and Anterior Pituitary Extracts. S. J. Folley, F. H. Malpress and F. G. Young.—p. 181.
Galactopoietic Action of Pituitary Extracts in Lactating Cows. S. J. Folley and F. G. Young.—p. 194.

Transactions Roy. Soc. Tropical Med. & Hyg., London

38:237-310 (March) 1945

*Amebiasis, with Special Reference to Treatment. A. R. D. Adams.—p. 237.
Tropical Ulcer. F. Marsh and H. A. Wilson.—p. 259.
*Survival of Transfused Red Cells in Blackwater Fever Circulation and of Blackwater Red Cells in Normal Circulation: Preliminary Report. H. Foy, A. Kondi, A. Rebelo and A. Soeiro.—p. 271.
Clinical Filariasis Due to Acanthocheilonema (Filaria) Perstans. E. I. Garratt.—p. 287.
Dividing Forms of Plasmodium Falciparum in Peripheral Blood of Africans. A. B. Raper, Margaret E. Wilson and D. B. Wilson.—p. 291.
*Massive Dose Tryparsamide by Intravenous Drip Method in Treatment of Trypanosomiasis. A. F. Fowler.—p. 297.

Treatment of Amebiasis.—According to Adams, large numbers of men overseas are being exposed to infection with Endameba histolytica. Some suffer from gross clinical attacks of amebic dysentery, others give no such history but are found to be infected on routine examination of the stools. The author thinks that it is improper to neglect a detected infection with E. histolytica until clinical manifestations make their appearance. To do so is to condemn many patients to subsequent unnecessary ill health with the possible development of a major disaster such as an amebic liver abscess. Furthermore, such patients are liable to disseminate the infections to others. They should be regarded as latent cases requiring early treatment. To discover these infections necessitates routine repeated stool examination. Emetine has a more specific action on this infection than any other drug. Emetine alone by injection will not sterilize an infection in more than a minority of cases; if it is given unwisely the infection becomes resistant to the drug in all forms and less amenable to treatment. Therefore the use of emetine by injection should be restricted to the control of clinically acute manifestations, and the minimum amount necessary to achieve this end should be given. The eradication of an intestinal infection must be attempted by the use of a variety of drugs, including emetine preparations, all of which have some action on the infection. These drugs should be given together because their combined effect is greater than that of any single drug alone, and they must be given as early as possible over an adequate period. Three weeks of such treatment ensures a high proportion of cures in cases not previously repeatedly treated subcuratively.

Survival of Transfused Red Cells in Blackwater Fever.—Foy and his associates found that red cells transfused from compatible group O donors into hemolyzing cases of blackwater fever were destroyed in the blackwater fever circulation just as were the patient's own cells. Red cells taken from a hemolyzing group O case of blackwater fever and transfused into a normal group A person had a survival time of only six days, indicating that there is some defect in the blackwater fever red cells that renders them more susceptible to destruction even in normal circulations. Plasma taken from a hemolyzing case of blackwater fever and transfused into a patient with an acute attack of malaria failed to produce signs of hemolysis. Normal red cells transfused into patients with hemolytic jaundice have a normal survival time but hemolytic jaundice cells transfused into normal circulations have a shortened survival time, indicating that in this disease the primary defect is in the red cells. The hemolytic processes in blackwater fever and hemolytic jaundice may be of a fundamentally different nature. Lysolecithin fragility is increased in both blackwater fever and hemolytic jaundice, making it appear that this may be a better guide to hemolytic tendencies than is saline fragility or spherocytosis.

Tryparsamide by Intravenous Drip.—The results obtained in the treatment of early syphilis by massive dose intravenous drip arsenotherapy prompted Fowler to treat cases of trypanosomiasis similarly, using the pentavalent arsenical tryparsamide. He employed the intravenous drip method in 42 consecutive cases of trypanosomiasis. This method requires hospitalization but reduces the time of treatment from twelve weeks or more to about twelve days or less. The method produces rapid sterilization of the blood and lymph nodes and it is unlikely that treated cases will become arsenic resistant. Children and young adults tolerate the treatment well. The aged are unsuitable for such treatment. Brief case histories are given of 24 patients who were examined from four to seven months after treatment. Although it is impossible to estimate the curative effect of the treatment without further examination of the cases over a period of eighteen months, the results in the 24 cases appear to be encouraging.

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Radiologic Study of Cecocolic Invagination of Adult. R.-J. Gilbert and J. Garcia-Caldéron.—p. 251.
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*Treatment of Leukemia with Artificial Radioactive Sodium. J. E. Thygesen, A. Videbaek and I. Villaume.—p. 305.
Cystic Form of Cancerous Metastases of Bone. B. Engfeldt.—p. 317.
Internal Biliary Fistulas: 2 Cases. E. Brandel.—p. 333.

Osteochondritis Dissecans of Head of Femur.—Hermodsson presents histories of 5 cases in which he made careful x-ray studies and reviews cases from the literature. He differentiates between primary and secondary cases of osteochondritis dissecans of the head of the femur. To the latter he assigns cases caused by disorders such as cretinism and fracture of the neck of the femur. He stresses that in all cases of primary osteochondritis dissecans there exist x-ray signs indicating that a more or less extended osseous aseptic necrosis was present in the head of the femur. He offers the following explanation of the pathogenesis: There exists an aseptic necrosis. This is not completely reorganized and a reduced resistance remains. Under the influence of strain or trauma a pathologic fracture results at the most exposed site of the femoral head, the upper pole. This engenders a limited aseptic necrosis and this in turn results in osteochondritis dissecans, as was shown by Axhausen. This theory of pathogenesis explains the fact that most of the patients are laborers. The author describes some cases which represent an intermediate form between Perthes' disease and osteochondritis dissecans and suggests that if Perthes' disease is designated as osteochondritis deformans or osteochondrosis deformans these intermediate forms should be designated as osteochondritis deformans dissecans or osteochondrosis deformans dissecans.

Treatment of Leukemia with Artificial Radioactive Sodium.—Thygesen and his associates gave intravenous injections of a solution of radio sodium, Na^{24}, to 7 patients with chronic lymphatic leukemia. Except in 1 of the cases, which later proved refractory also to roentgen treatment, the fall in the white cell counts and the remissions obtained were similar to those after exposure to roentgen rays. The patients showed subjective as well as objective improvement. In 2 of the patients the improvement has been manifest for several months, but otherwise the time is too short to be able to judge the duration of the effect. In addition to the 7 cases of leukemia, 1 case of polycythemia vera was treated with radio sodium; here the effect was slight and only temporary.

Book Notices

Clinical Cystoscopy: A Treatise on Cystoscopic Technic, Diagnosis, Procedures, and Treatment. By Lowrain E. McCrea, M.D., F.A.C.S., Associate Professor of Urology, Temple University Medical School, Philadelphia. In two volumes. Drawings by B. Engle Shaffer. Cloth. Price, $25, per set. Pp. 534; 535-1056, with 667 illustrations. Philadelphia: F. A. Davis Company, 1945.

This treatise on clinical cystoscopy is a thorough presentation on the subject in two beautifully printed volumes. The classification of the text is good. The chapters are well arranged, carefully balanced and properly organized. The volumes read easily and are profusely illustrated. The drawings, paintings and photography, especially the colored photography of the cystoscopic appearance of the bladder diseases, are superb.

In the first volume are seventeen chapters, the first four of which take up the history of the cystoscope, the various types of cystoscopic instruments, indication and contraindication for cystoscopy, preparation of the patient for cystoscopy and the method of performing a cystoscopy. In chapter five the cystoscopic picture of the normal bladder is discussed. In the next seven chapters all the known diseases of the bladder are considered and these are discussed in a thorough, concise manner. Beautiful paintings or colored photographs illustrate the cystoscopic pictures of the disease. A chapter on the neurogenic bladder follows with a good classification of these disturbances, supplemented by various forms of treatment. In the chapter on prostatic hypertrophy the author's opinions concerning the indications and contraindications for transurethral resections may not be acceptable for many other urologists. The last three chapters discuss the ureter: its anomalies and diseases.

In the second volume are fourteen chapters in which surgical and medical diseases of the kidneys are discussed. One entire chapter is devoted to the subject of kidney function tests. Urology in children and the female requires two chapters for its comprehensive presentation. The last chapter concerns roentgenography in urology. More consideration might have been given to excretory urography. For instance, little effort has been made to discuss the physiologic principles of this diagnostic procedure. There are those who are not in complete agreement with the author in his discussion of the comparative value of retrograde and excretory pyelograms. At the end of each volume is an extensive and authentic bibliography arranged to coincide with the chapters.

These two volumes give the best presentation on clinical cystoscopy that the reviewer has seen and can be highly recommended to those interested in or desiring to learn more about cystoscopy. Even the trained cystoscopist can find much of value in them.

Penicillin hakkında in vitşo arastirmalar I-III (Almanca bölüm). Penicillin-Studien in Vitro I-III. Von Julius Hirsch, Hygiene-Institut der Universität Istanbul. Compte rendu annuel et archives de la Société turque des sciences physiques et naturelles, Fasc. 12 (Separatum). Paper. Pp. 88, with illustrations. Istanbul, 1945.

The monograph by Professor Hirsch deals with the author's theory of the mode of action of penicillin, the manometric test of penicillin activity developed by him and with a method of growing crude penicillin. Hirsch demonstrated in his experiments in vitro that penicillin has neither bactericidal nor bacteriostatic effect. Penicillin was shown to exert an effect only in bacterial cultures capable of multiplying. This effect becomes evident after multiplication of the bacteria has progressed for some time. In proportion to the added concentration of penicillin, the multiplication sooner or later suddenly changes into a logarithmically progressing process of destruction which may lead to lysis of the staphylococci. Generation of cells which develops in the presence of penicillin is incapable of further multiplication and their individual life span is abnormally short. These staphylococci show the morphologic changes described by Gardner. This effect of penicillin on the staphylococcus culture is a qualitative rather than a quantitative effect; it results in a generation of abnormal, sterile cells which rapidly die. The author considers this a specific action of penicillin and designates it as the "degenerative effect." This degenerative effect is characterized by a respiratory curve which, following the addition of penicillin, continues to increase for a while in normal logarithmic progression. The degenerative effect is the only effect of penicillin: a carefully purified barium salt produces exclusively this specific degenerative effect over a wide range of concentration (from 0.08 to 50.0 units per cubic centimeter). Hirsch also showed that in unpurified penicillin-barium salt a second antibiotic factor exists. This factor has a typical bacteriostatic action. It accompanies penicillin in the culture filtrates of penicillium notatum Fleming. The interference by this factor with the specific effect of penicillin is quite evident even in diluted crude penicillin.

The manometric penicillin test developed by the author depends on the respiration rate (oxygen consumption—by time unit) of staphylococcus cultures in the presence of penicillin. The addition of penicillin to staphylococcus cultures results in an increase which is limited in time and is followed by logarithmic decrease. The oxygen deficit can be utilized for the determination of the activity of crude penicillin and of penicillin preparations.

Hirsch found that the addition of concentrated watery extracts of wheat bran to the Czapek-Dox medium (5 to 7.5 per cent of wheat bran or BK dry substance in the culture medium) produces in from eleven to twelve days a crude penicillin with from 50 to 60 units per cubic centimeter. A good penicillin crop can be obtained only in small cultures with limited surface. He was able to overcome the inhibition of the surface growth of the fungus by the method of a closed screen of floating glass bulb rods. By this method it is possible to produce mass cultures of the Fleming strain on culture mediums that contain wheat bran extract and that are of any desired surface. They produce, after eight days, a crude penicillin of at least 50 to 60 units per cubic centimeter.

This monograph is an important contribution to the new science of antibiotics. Although published in Turkey, it is written in German and should therefore be accessible to workers in this field.

Anatomy and Physiology for Students of Physiotherapy, Occupational Therapy and Gymnastics. By C. F. V. Smout, M.D., M.R.C.S., L.R.C.P., Senior Lecturer and Acting Professor, Department of Anatomy, University of Birmingham, and R. J. S. McDowall, M.D., D.Sc., Professor of Physiology, University of London, King's College. Cloth. Price, $8. Pp. 418, with 288 illustrations. Baltimore: William Wood & Company, 1944.

The authors state that this book is not intended to be used as a substitute for the standard anatomy and physiology textbooks. The amount of significant information presented in the volume, however, would hardly warrant its general use as a supplementary textbook. The cost of the book may be prohibitive for students. The most instructive chapters are those entitled Living Anatomy and Muscles in Action. The physical therapist, occupational therapist and teacher of physical education need a concentrated and sufficiently detailed diagrammatic and photographic presentation of surface anatomy as it applies to these fields. This section is well done but not complete. The chapter Muscles in Action is interesting for the diagrammatic and outline presentation of muscle function in common activities. The book would be more valuable if this section had been considerably enlarged. The section on physiology is not sufficiently related to the three fields under consideration to be of value as supplementary material, nor does it cover the subject thoroughly enough for a basic textbook.

Health Research in Industry. (Proceedings of a Conference on Industrial Health Research held at the London School of Hygiene and Tropical Medicine, 28th September, 1944.) Medical Research Council, Industrial Health Research Board. Paper. Price, 6d. Pp. 27. London: His Majesty's Stationery Office, 1945.

This bulletin contains a series of papers presenting the views of the Medical Research Council and of management, medicine and trade unions on the present state of organization and desirable evolution of industrial health services. The opinions expressed indicate that at least in respect to health matters not much controversy remains. Neglect of manpower is poor business—and there no longer is room in competitive industry for the bad manager. Labor asks for liberalization of occupational disease benefits, better working environment and intensified research. The organization and early experiences of the Department of Research on Industrial Medicine of London Hospital are described, as is also the work of the applied psychology unit of Cambridge University.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

DIAGNOSIS OF THYROTOXICOSIS

To the Editor:—I should appreciate comment on the following statement, the origin of which I cannot find but the value of which I believe to be significant: "Any patient with hyperthyroidism has a tachycardia while sleeping and has a widened pulse pressure. If the pulse at rest is normal and/or if the blood pressure is normal, the diagnosis of thyrotoxicosis is excluded." MC, U.S.N.

ANSWER.—The statement that a normal pulse rate and a normal blood pressure at rest exclude the diagnosis of thyrotoxicosis is true in most instances but not in all. In making the diagnosis of toxic goiter it is not sufficient to rely on the pulse rate and blood pressure, and there is too much tendency at the present time to do so; for example, one pharmaceutical house recently considered the desirability of distributing among physicians a chart for determining the basal metabolic rate from the product of the pulse pressure and the pulse rate. The diagnosis of thyrotoxicosis is usually not difficult, but in doubtful cases attention must be paid to many factors and it is sometimes necessary to observe the response of the basal metabolism to iodine or thiouracil before arriving at a definite conclusion.

SMOKING IN PULMONARY TUBERCULOSIS

To the Editor:—In the book of instructions to patients at a tuberculosis institution it is stated that tobacco is injurious to patients with tuberculosis of the lungs. Many practicing physicans apparently disagree with this opinion. Is there any authentic work on this subject? M.D., Virginia.

ANSWER.—Statistical studies have not shown tuberculous infection or disease to be more frequent in users of tobacco than in those who abstain. Well controlled quantitative studies of the effect of tobacco on the course of pulmonary tuberculosis are lacking. Among tuberculous patients it has been found that those who smoke are apt to have a higher incidence of laryngeal involvement and that such complications appear to be adversely affected by persistence in smoking. Acceleration of the pulse rate, frequent extrasystoles and accentuated sinus arrhythmia, hacking cough, hoarseness and diminished appetite, which so often result from tobacco smoking, may simulate or even accentuate the symptoms of tuberculosis, whether or not they exert much influence on the actual course of the disease in the average patient. The course of pulmonary tuberculosis is so variable and is influenced by so many factors that it is not easy to demonstrate an important or clearcut effect from any one item or detail in the regimen of treatment. Most phthisiologists, however, are convinced that smoking can do no good and may do harm sufficiently often to advise against it.

References:

Bogen, Emil: Tobacco and Tuberculosis, *Dis. of Chest* **3**: 22 (March) 1937.

Schrumpf-Pierron, P.: Tobacco and Physical Efficiency, New York, Paul B. Hoeber, 1927.

EXSTROPHY OF BLADDER

To the Editor:—How early in life may a child be operated on safely for exstrophy of the bladder? L. Edward Giovine, M.D., Woodside, N. Y.

ANSWER.—The operation for exstrophy of the bladder which is generally accepted consists in reimplantation of the ureters into the sigmoid, with excision of the vesical tissue. There is some difference of opinion as to the most favorable age at which a child should be operated on. Many surgeons have waited until the child is 3 or 4 years of age before advising operation. Recently operation has been advised for infants less than 1 year of age; in fact, preferably under 6 months. The reasons given are (1) to avoid the possibility of ascending infection, (2) tolerance to operation by the infant and (3) to obviate the psychologic impression of physical defect on the older child. Some surgeons however believe that, because of diminutive size of the ureteral and other tissues, the technical difficulties are greatly increased in infancy. It is open to question whether serious pathologic complications in the urinary tract develop often prior to 3 years of age.

HOMOSEXUALITY

To the Editor:—Is homosexuality thought to be a congenital or an acquired condition? Paul Sizemore, M.D., Durant, Okla.

ANSWER.—Despite the fact that some homosexuals have rather obvious characteristics of the opposite sex both in physical appearance and in character traits, the majority of psychiatrists and sexologists believe that homosexuality is an acquired condition and that the main etiologic factors are psychogenic rather than genetic.

All human beings are to varying degrees bisexual, and under certain environmental circumstances homosexual behavior may break out in persons whose previous behavior has been consistently heterosexual. This phenomenon is not uncommon in men confined to a completely homosexual environment as, for example, a prison, or among adolescents living in institutions limited to one sex.

Many homosexuals have had or are capable of having heterosexual experiences. During psychiatric treatment it is learned that the homosexual has the usual heterosexual wishes and longings but these are repressed because of deep seated fears of heterosexuality. Childhood sexual experiences of a fearful nature, especially parental attitudes which are prohibitive, threatening and punitive toward the normally developing sexuality (the expression of sexual curiosity and sexual play such as masturbation) may in the child shift the scale toward homosexuality. As such a child grows up he retreats from heterosexuality to homosexuality because of previous fearful associations with heterosexuality.

A recent study of hermaphrodites by Ellis (The Sexual Psychology of Human Hermaphrodites, *Psychosomatic Med.* **7**:108 [March] 1943) has thrown more light on the importance of psychogenic and environmental factors in homosexuality. He found that the hermaphrodite assumes the sexual role that accords primarily not with his or her internal or external somatic characteristics but rather with his or her masculine or feminine upbringing. Therefore heterosexuality and homosexuality in hermaphrodites as in the nonhermaphrodite are primarily caused by environmental and not by endocrine or other physiologic factors.

Although the treatment of homosexuality is a difficult task, thoroughgoing psychiatric treatment which aims at uncovering and correcting psychogenic factors offers a much better hope for cure than treatment with injections of endocrine preparations.

TOXICITY OF CHLORINATED NITRILS

To the Editor:—Could you give me any information regarding the toxicity of chlorinated nitrils? F. F. Boys, M.D., East Chicago, Ind.

ANSWER.—It was shown by Liese (*Ztschr. f. hyg. Zool. Schädlingsbek.* **33**:1, 1941; *Chem. Zentralbl.* **1**:2713, 1941) that trichloracetonitrile (CCl_3CN) is somewhat less toxic than sulfur dioxide in that a concentration of 2.9 Gm. per cubic meter (490 parts per million) was comparatively well tolerated by mice, whereas sulfur dioxide in concentrations of 2.76 Gm. per cubic meter (1,031 parts per million) was absolutely fatal.

According to Meurice (*Arch. internat. pharmacod.* **7**:11, 1900) the fatal dose of chloral nitrile ($CCl_3CH(OH)CN$) with subcutaneous injection for pigeons is 0.012 mg. per gram of body weight and that of the corresponding nonhalogenated nitrile (lactonitrile, $CH_3CH(OH)CN$) is 0.010 mg. per gram of body weight, whereas that of potassium cyanide is 0.0015 mg. per gram of body weight. Hunt (*Arch. internat. pharmacod.* **12**:497, 1904) determined the fatal dose of chloral nitrile with subcutaneous injection for mice as 0.023 mg. per gram of body weight, whereas the fatal dose of hydrocyanic acid was 0.005 mg. per gram of body weight. It appears, therefore, that the chlorinated nitrile is of the same order of toxicity as the unsubstituted nitrile and that both are about five times less toxic than hydrocyanic acid, causing the same or at least a similar toxicologic picture.

CONVULSIONS IN CHILDREN

To the Editor:—Do children with chorea ever have convulsions? Are there any other conditions that are accompanied by the emotional and physical disturbances associated with chorea? M.D., Ohio.

ANSWER.—Convulsions are not usually a symptom or a part of chorea in children. Although a convulsive seizure may usher in the onset of an acute chorea, it is hardly ever seen as a part of it. There are other conditions that may have convulsive seizures in association with choreiform movements. These are encephalitis, meningoencephalitis, lesions of the corpus luysi (hemiballisms) and various degenerative diseases of the basal ganglions.